Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Insights into selenylation of imidazo[1,2-*a*]pyridine: synthesis, structural and antimicrobial evaluation

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General procedure for synthesis of 3: The compounds **3a-c** were synthesized by earlier reported method[1]. To a solution of chloroacetic acid (3.67g, 38.8mmol) in water (6ml), triethyl amine was added (6.12 ml, 44 mmol) dropwise at room temperature. After 10 minutes of stirring 2-aminopyridine (4.3 g, 46mmol) was added and was refluxed at 90^0C for 5h. Then reaction mixture was cooled to room temperature, ethanol was added and stirred at 5^0C for 2h to obtain precipitates which were filtered, washed with cold ethanol (4ml), dried to get 5.3g (89%) of intermediate **2a**. This intermediate **2a** (5.3g, 34.8 mmol) was dissolved in toluene (25 ml) and phosphorous oxychloride (9.7 ml, 104 mmol) was added dropwise at reflux. After refluxing for 16 h reaction mixture was cooled to room temperature and cold water (100 ml) was added, stirred for 15minutes. Aqueous layer was separated and neutralized with 10% NaOH (aq) and the precipitate was filtered and dissolved in dichloromethane. The aqueous filtrate was also extracted with dichloromethane (4x20ml). The combined organic layers were washed with brine, dried over anhydrous sodium sulphate and concentrated under vacuum to afford a brown powder. This was purified column chromatography on silica gel using hexane: ethyl acetate (90:10) as eluent to yield 5.2g (98%) of 2-chloroimidazo[1,2-a]pyridine (**3a)**. 2-chloro-7-methylimidazopyridine (**3b**) and 2-chloro-7-methylimidazopyridine (**3c**) were prepared similarly by using 2-amino-4-picoline and 2-amino-5-picoline respectively.

2-Chloroimidazo[1,2-a]pyridine (3a): Yield: : 74.6%, white crystalline solid, m.p. 76–77^0C, ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.95 (d, *J* = 6.8 Hz, 1H), 7.39 (t, *J* = 4.3 Hz, 2H), 7.09 (ddd, *J* = 9.1 Hz, *J* = 6.9 Hz, *J* = 1.2 Hz, 1H), 6.71 (td, *J* = 6.8 Hz, *J* = 0.9 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 143.7, 135.5, 125.1, 116.8, 112.9, 108.1

2-Chloro-7-methylimidazopyridine (3b): Yield: 72.4%, white crystalline solid, m.p. 85–87^0C ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.89 (d, *J* = 6.9 Hz, 1H), 7.38 (s, 1H), 7.22 (s,

1H), 6.62 (dd, *J* = 6.9 Hz, *J* = 1.5 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 144.1, 136.2, 135.0, 124.3, 115.4, 115.2, 107.4, 21.2

2-Chloro-6-methylimidazopyridine (3c): Yield: 73.8%, white crystalline solid, m.p. 90-93^{0}C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.26 (t, *J* = 4.6 Hz, 2H), 6.91 (dd, *J* = 9.3, 1.6 Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 142.6, 134.9, 128.2, 122.9, 122.6, 116.0, 107.8, 17.9

General procedure for synthesis of 4a-c: Compounds **3a-c** (40mmol) was added to dimethylformamide (60 ml) under ice bath at 5^{0}C. To this solution, phosphorous oxychloride (6 ml) was added dropwise. After addition reaction was allowed to stir at room temperature for 2h. The reaction mixture was poured onto crushed ice and precipitates were filtered by vacuum filtration and dissolved in dichloromethane. This organic layer was dried on anhydrous sodium sulphate and concentrated under vacuum to yield corresponding product **4a-c**.

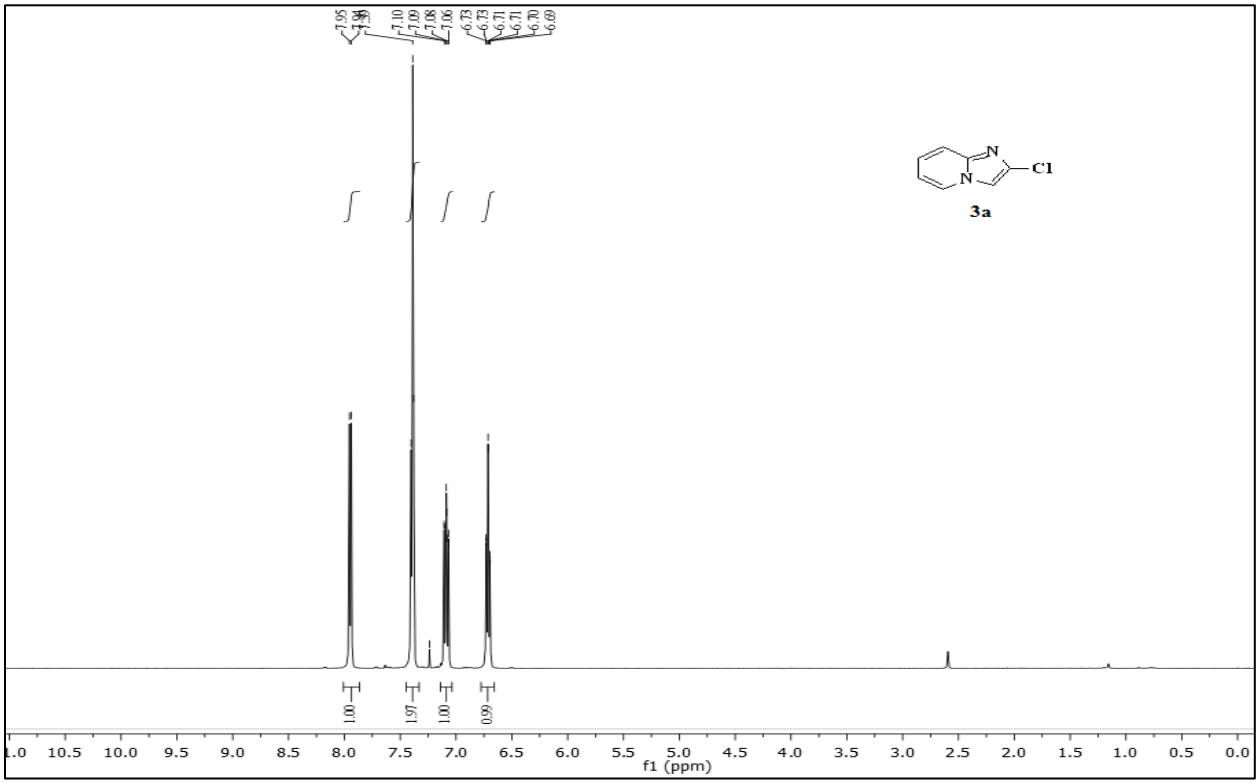
2-Chloro-3-formylimidazo[1,2-a]pyridine (4a): Yield: 88%, white crystalline solid, m.p. 110-111^{0}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 9.35 (d, *J* = 6.8 Hz, 1H), 7.59 (d, *J* = 8.9 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.08 (td, *J* = 6.9, 1.2 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 176.9, 147.2, 146.0, 130.8, 127.9, 118.6, 116.9, 115.9.

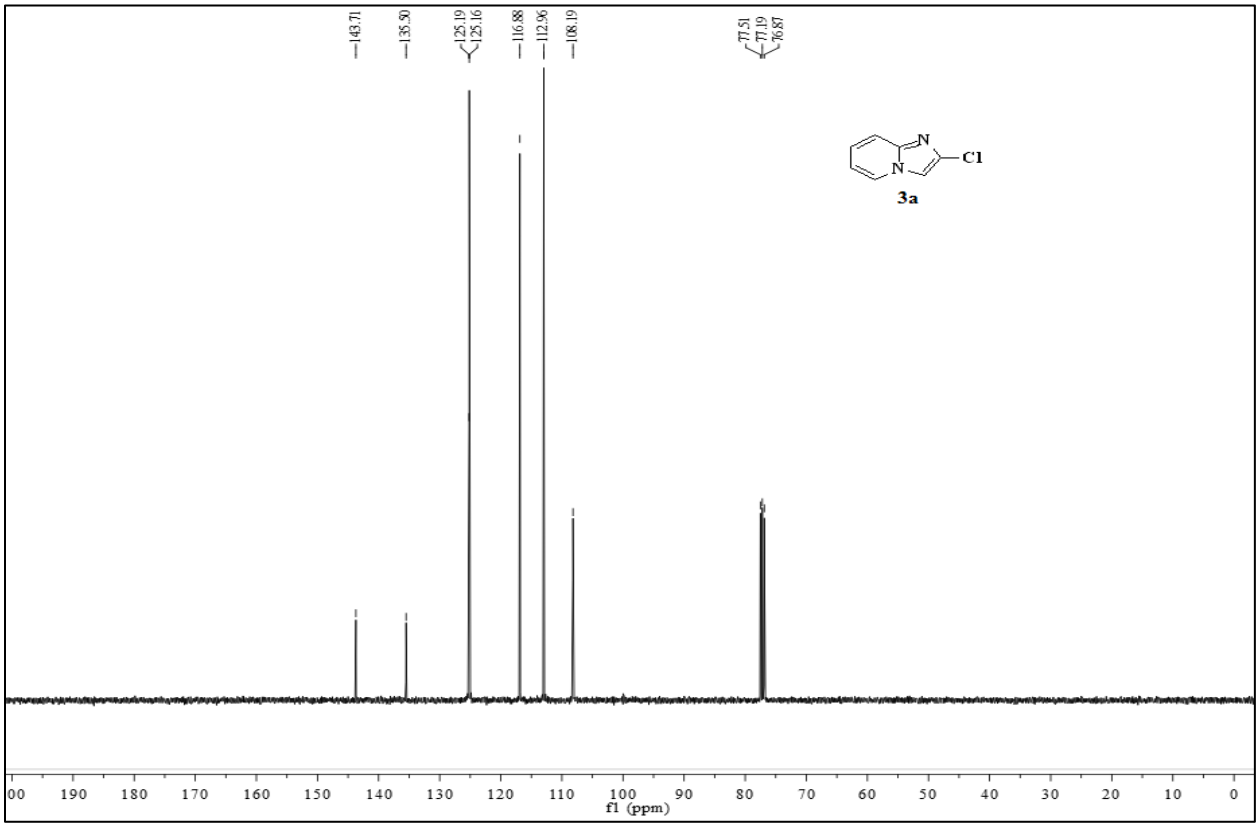
2-Chloro-3-formyl-7-methylimidazopyridine (4b): Yield: 87%, white crystalline solid, m.p. 115-117^{0}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 9.20 (d, *J* = 6.9 Hz, 1H), 7.34 (s, 1H), 6.90 (dd, *J* = 6.9, 1.6 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 176.6, 147.4, 146.5, 142.8, 127.1, 118.8, 118.4, 115.7, 21.7

2-Chloro-3-formyl-6-methylimidazopyridine (4c): Yield: 87%, white crystalline solid, m.p. 114-115^{0}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 9.17 (s, 1H), 7.48 (d, *J* = 9.1 Hz,

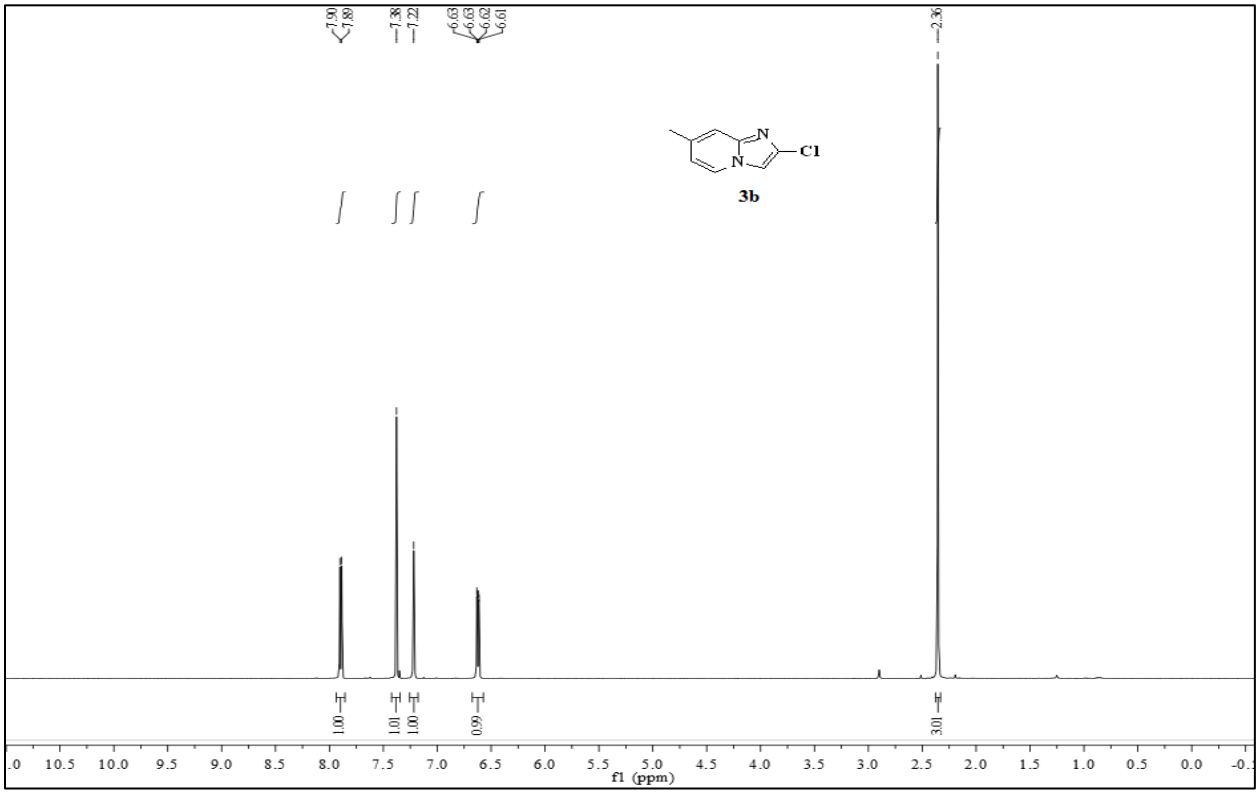
1H), 7.35 (dd, *J* = 9.1, 1.5 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ (ppm): 176.8, 146.9, 144.9, 133.6, 126.3, 126.0, 118.4, 116.1, 18.2

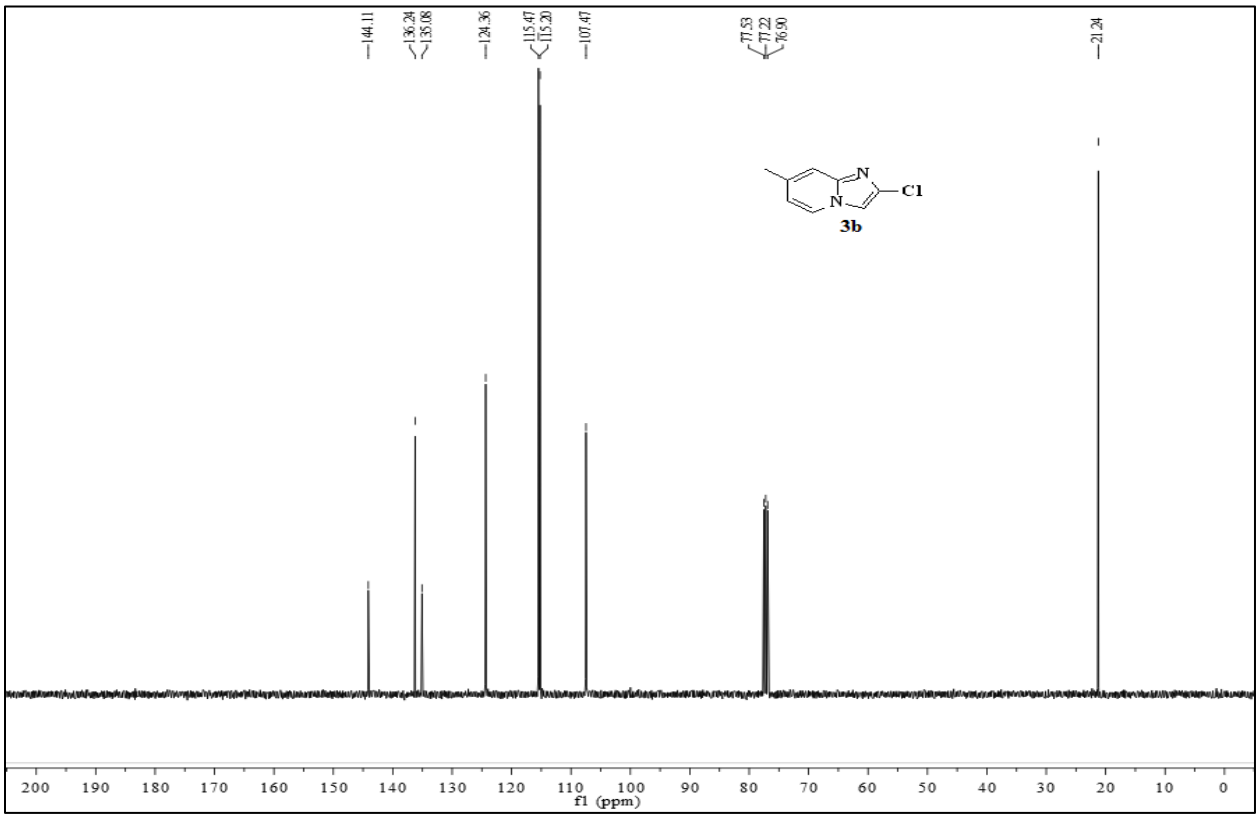
^{1}H, ^{13}C-NMR of 2-Chloroimidazo[1,2-a]pyridine (3a)



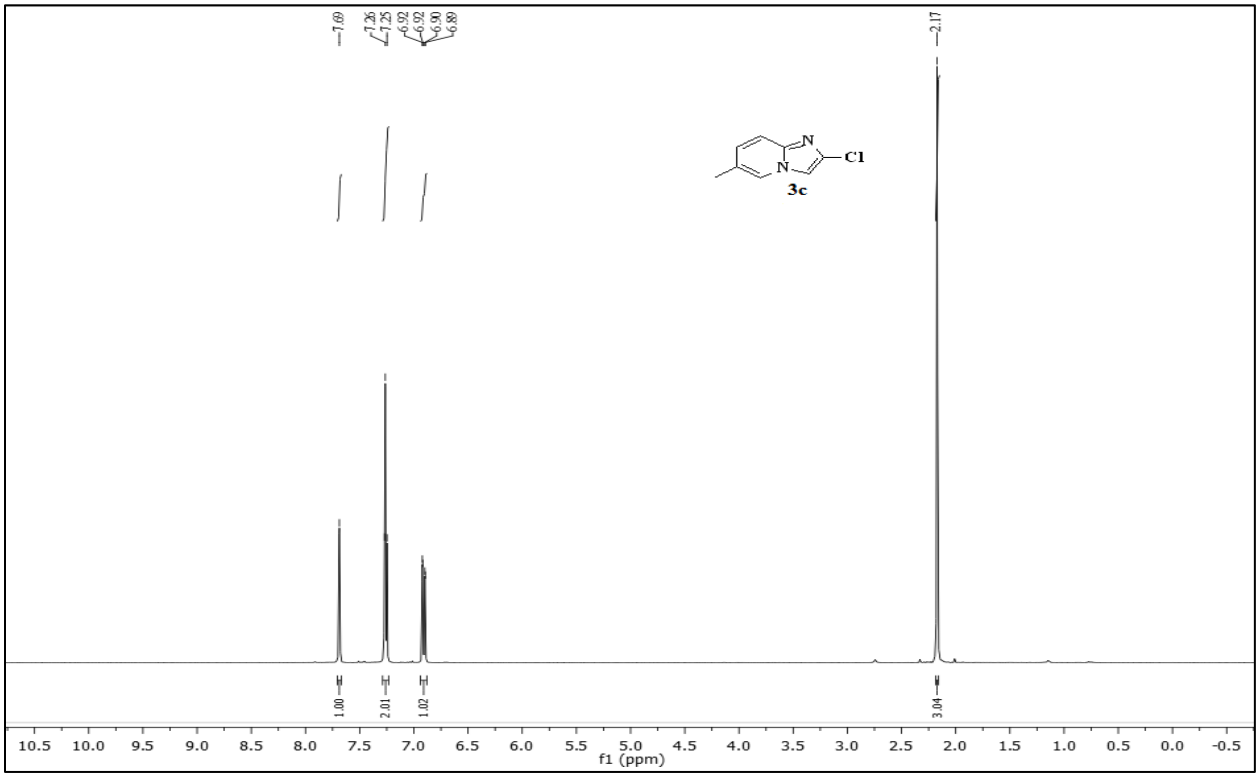


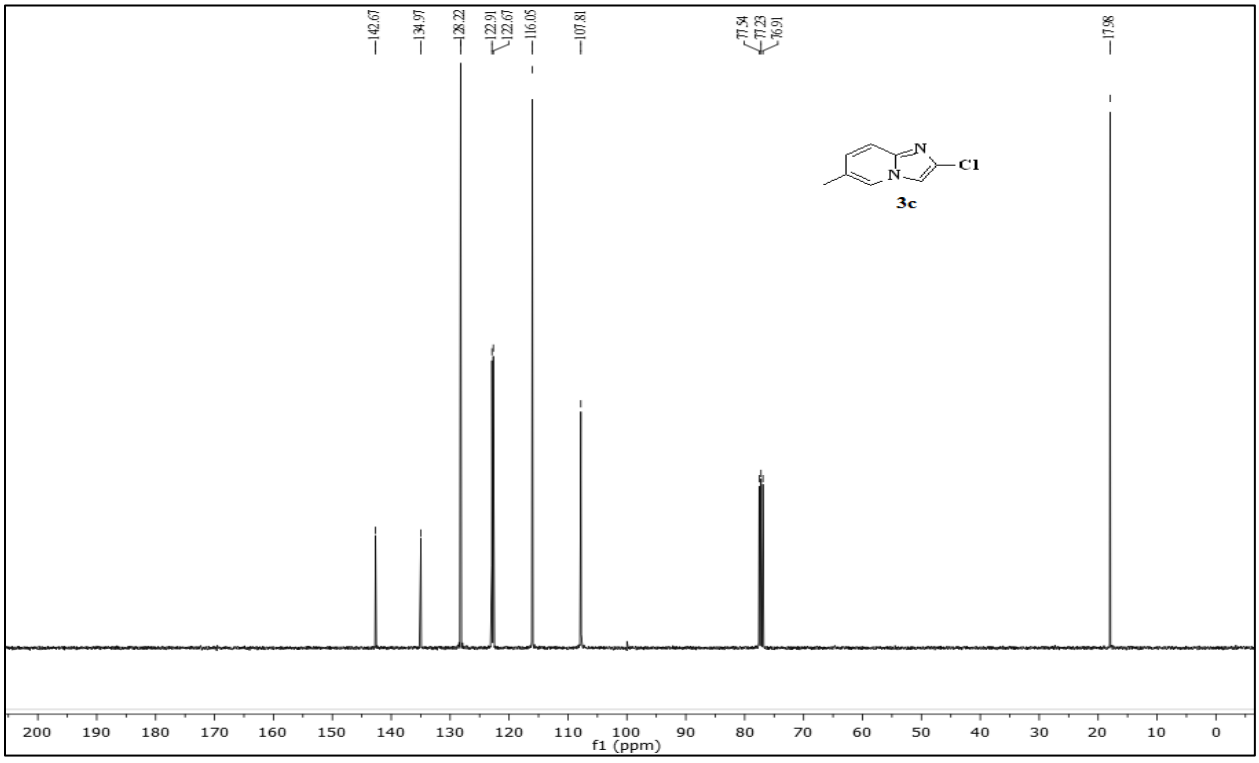
^{1}H, ^{13}C-NMR of 2-Chloro-7-methylimidazopyridine (3b)



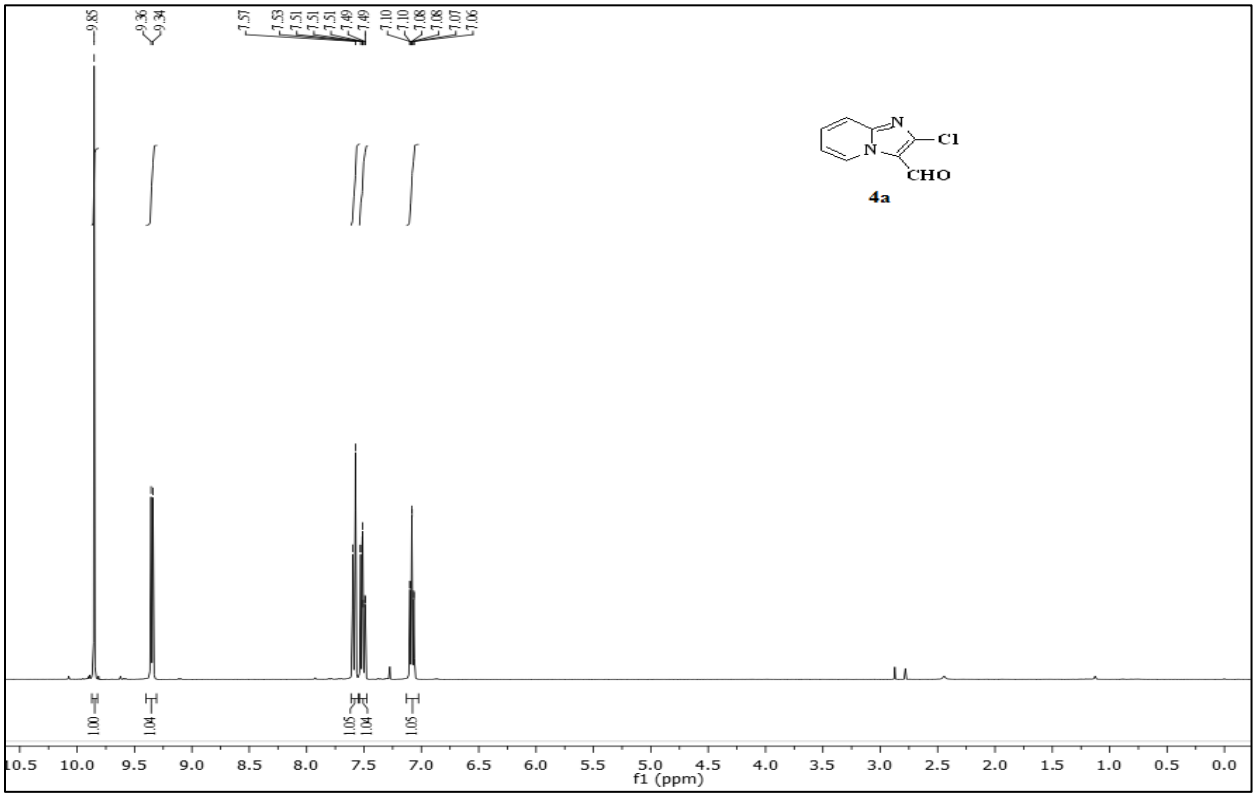


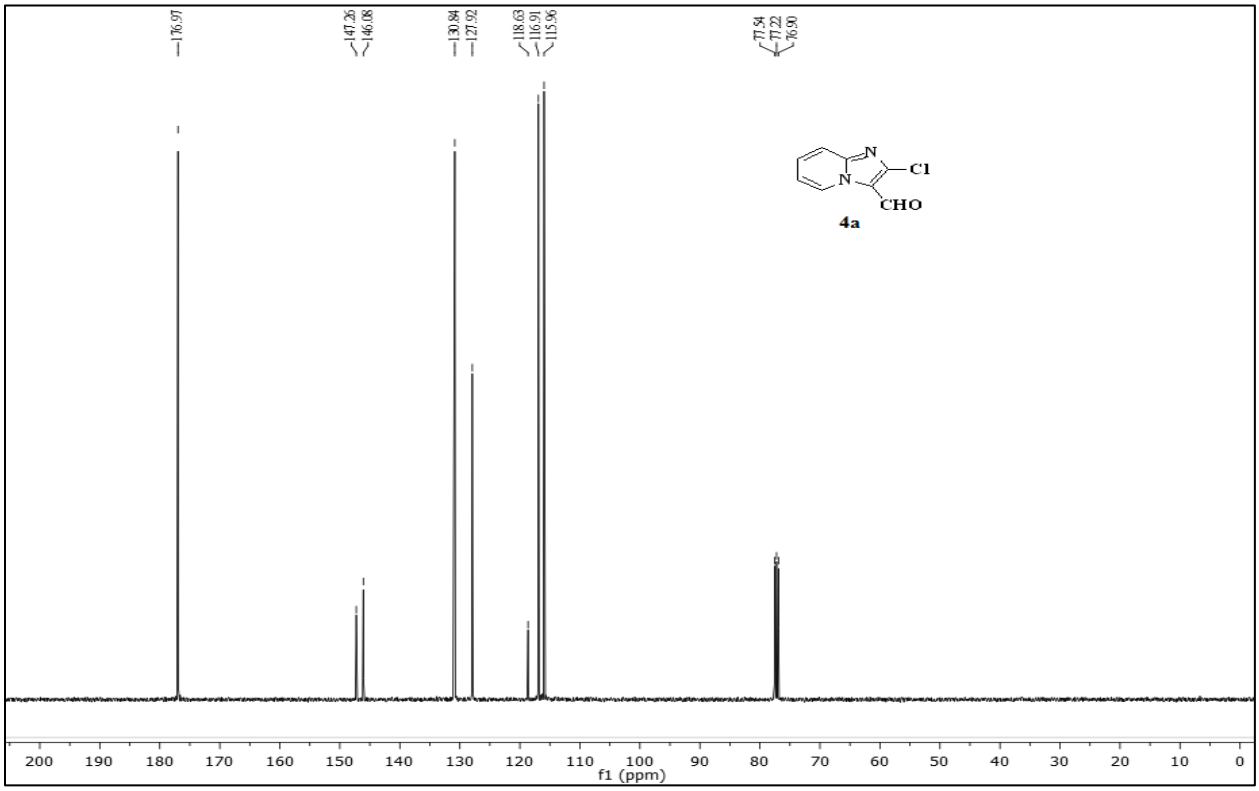
^{1}H, ^{13}C-NMR of 2-Chloro-6-methylimidazopyridine (3c)



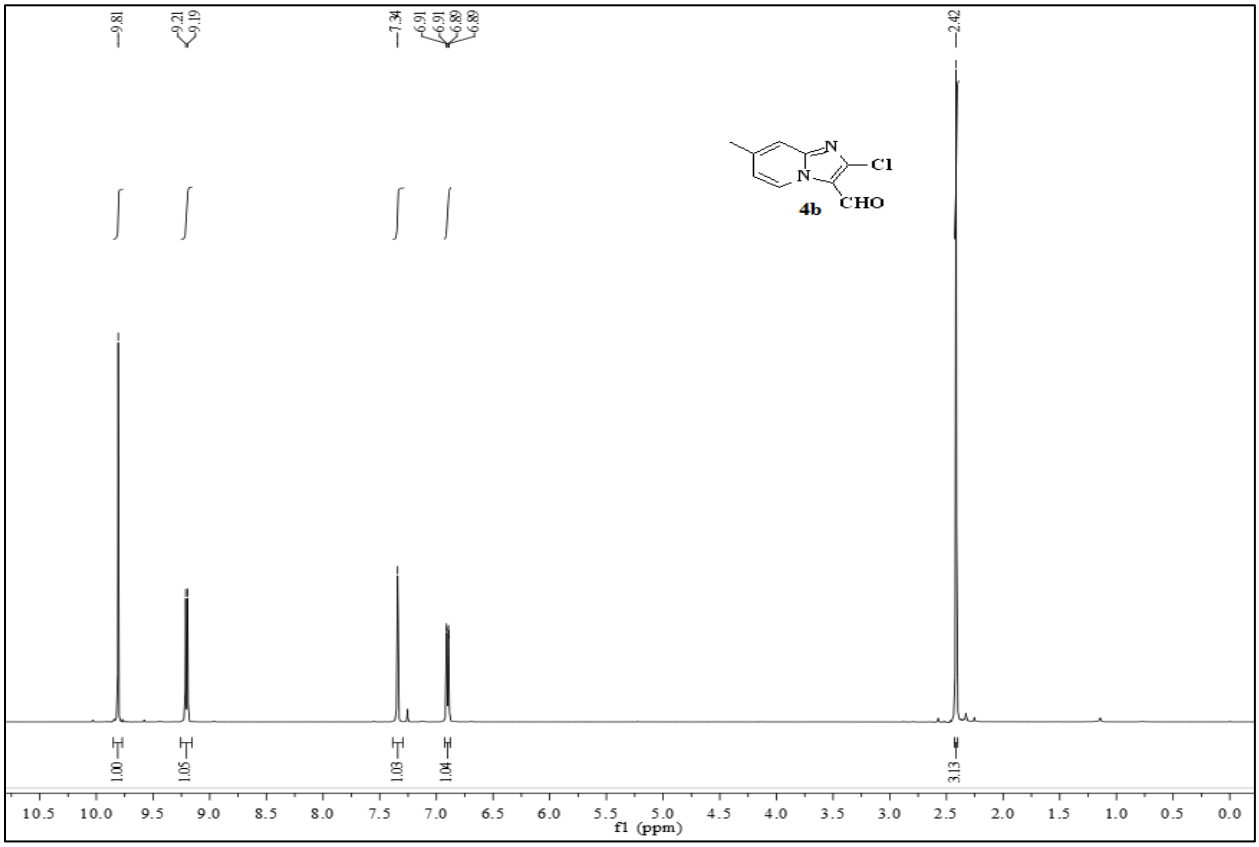


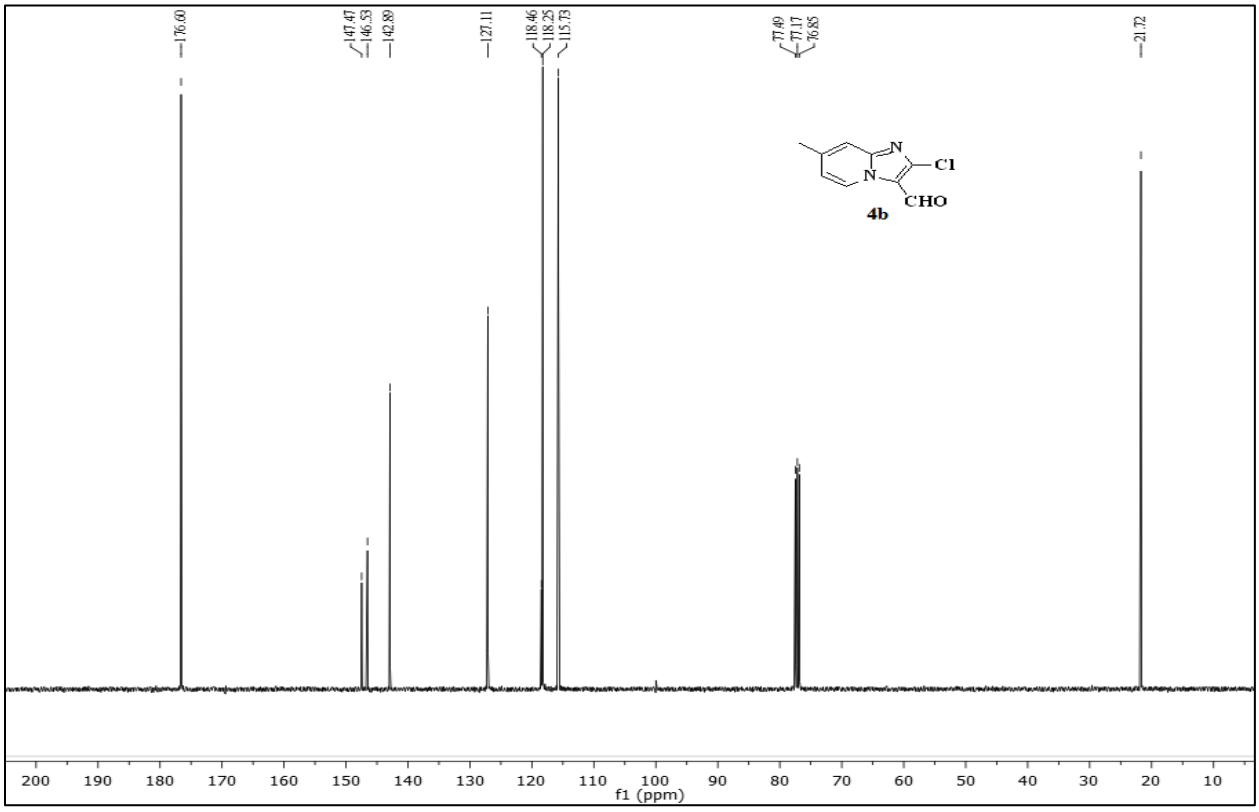
^{1}H, ^{13}C-NMR of 2-Chloro-3-formylimidazo[1,2-a]pyridine (4a)



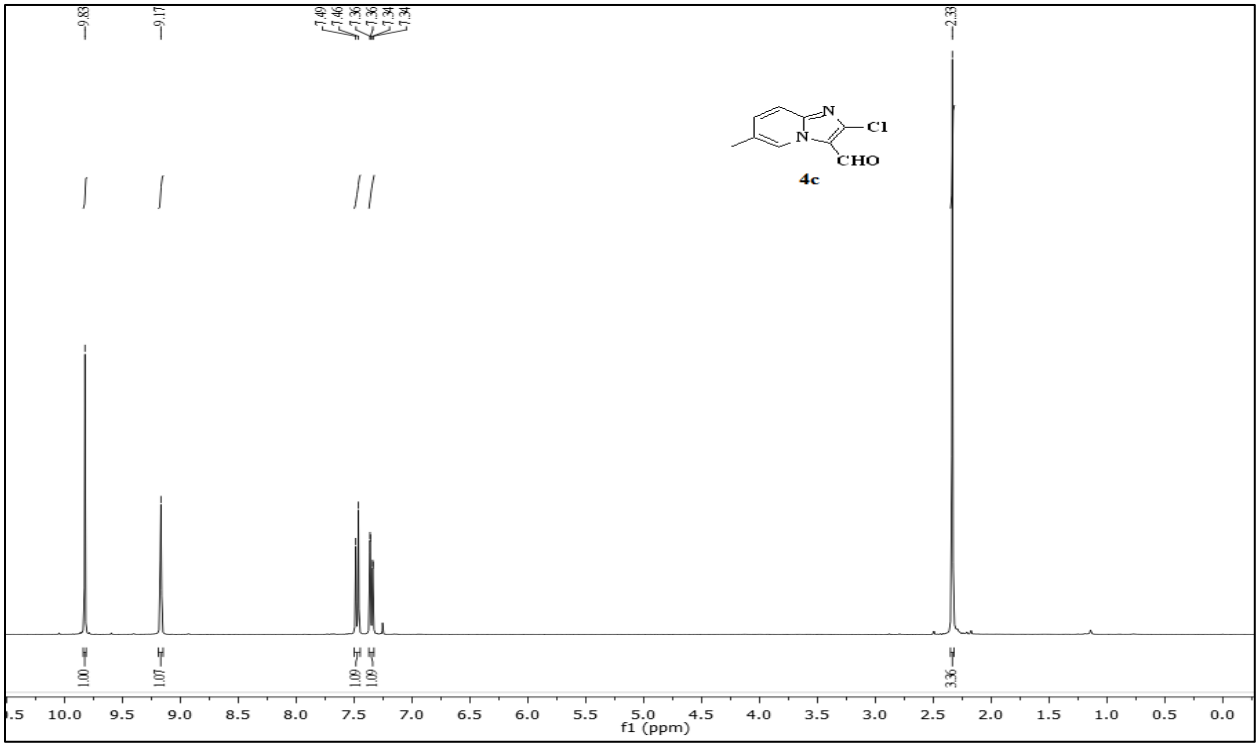


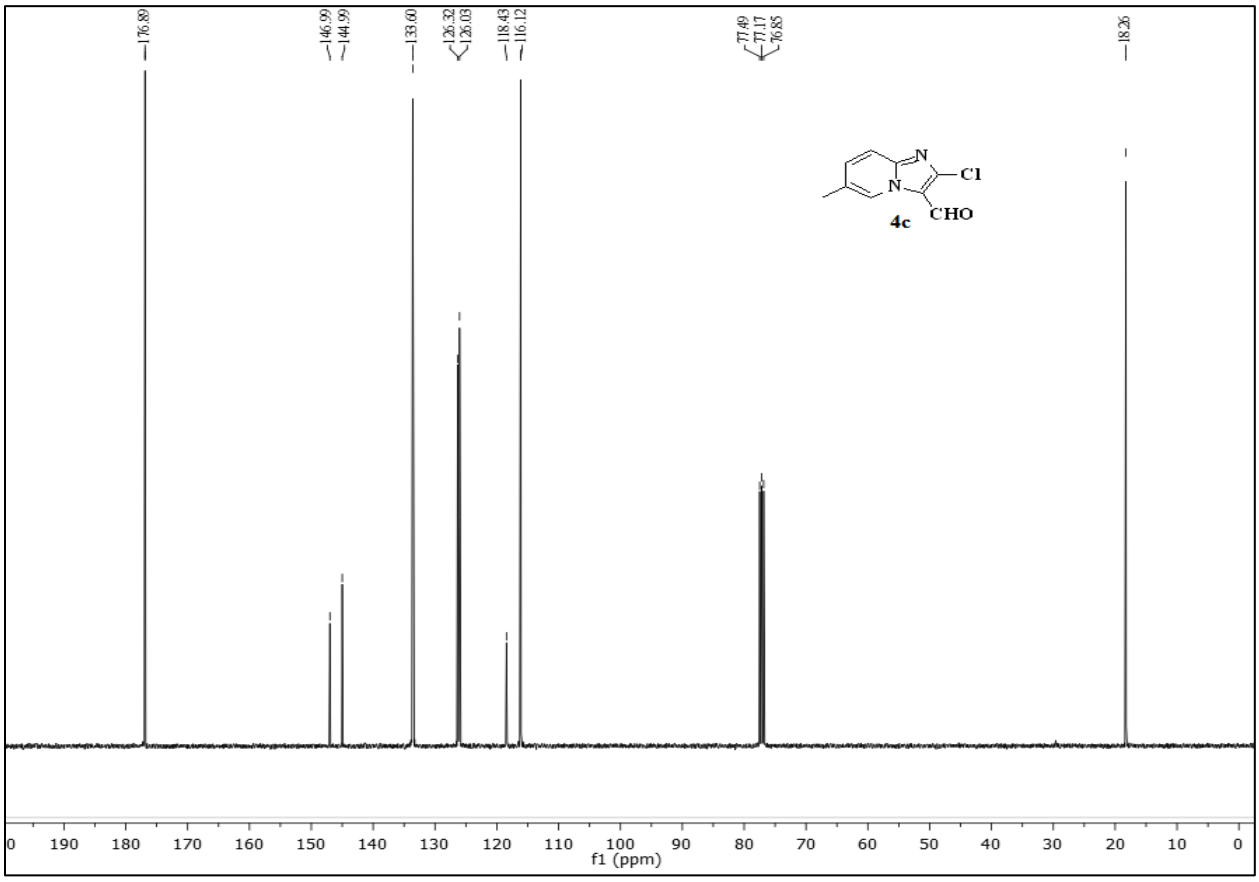
^{1}H, ^{13}C-NMR of 2-Chloro-3-formyl-7-methylimidazopyridine (4b)



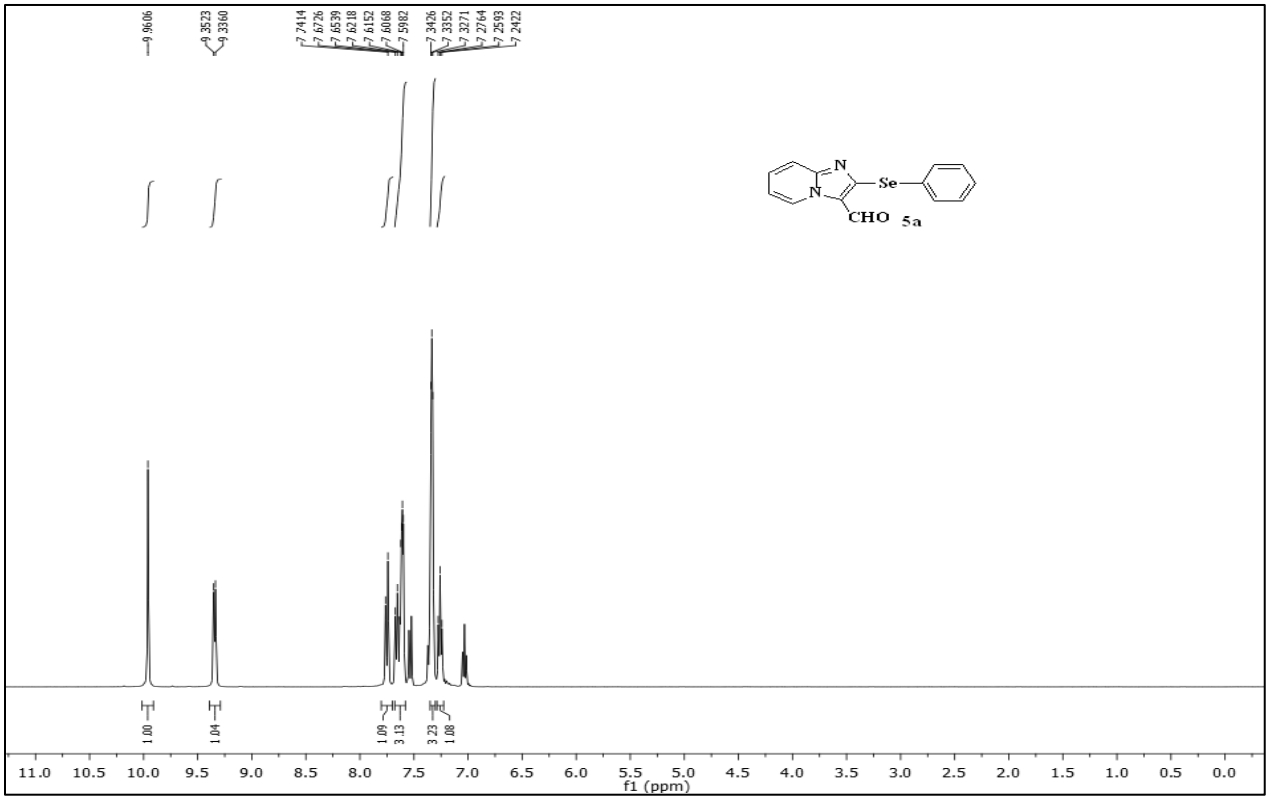


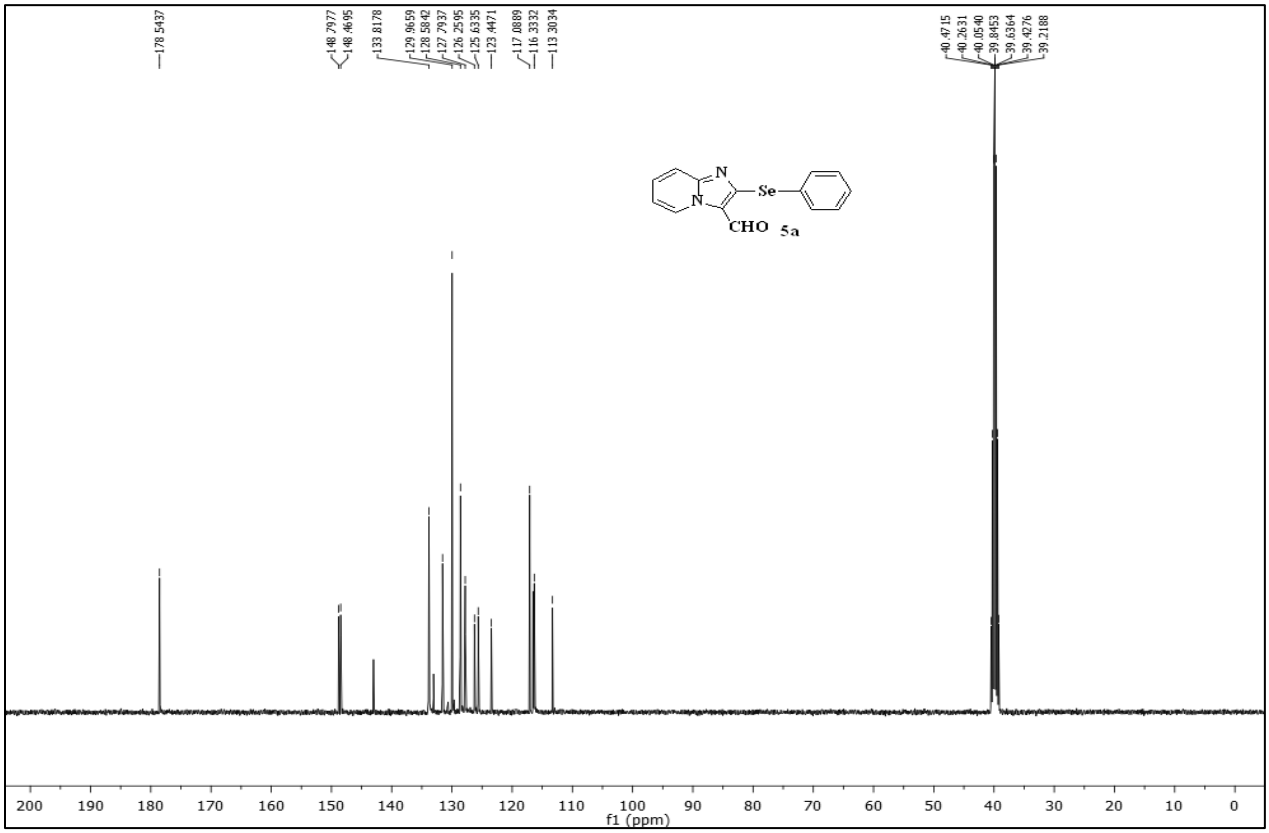
^{1}H, ^{13}C-NMR of 2-Chloro-3-formyl-6-methylimidazopyridine (4c)

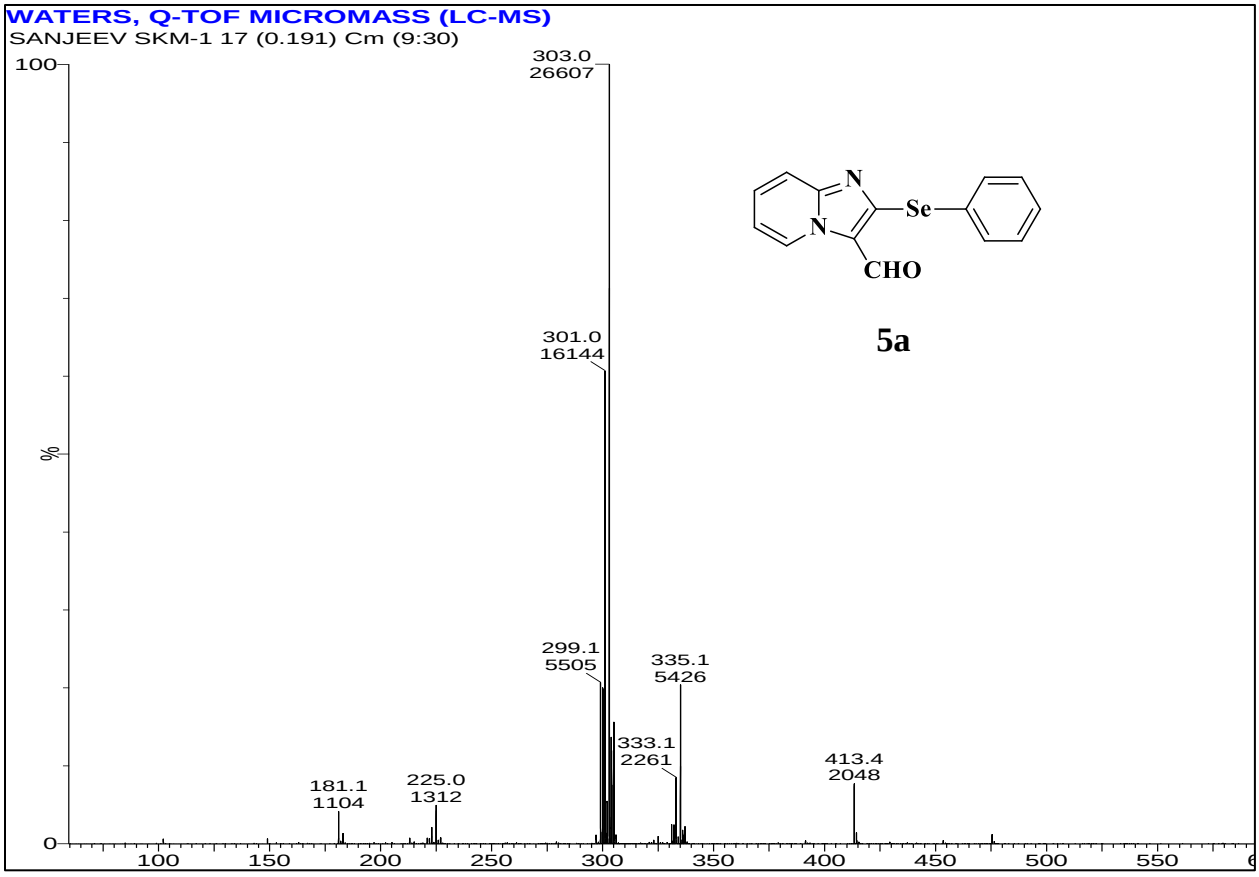




^{1}H, ^{13}C-NMR of 2-(o-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5a)

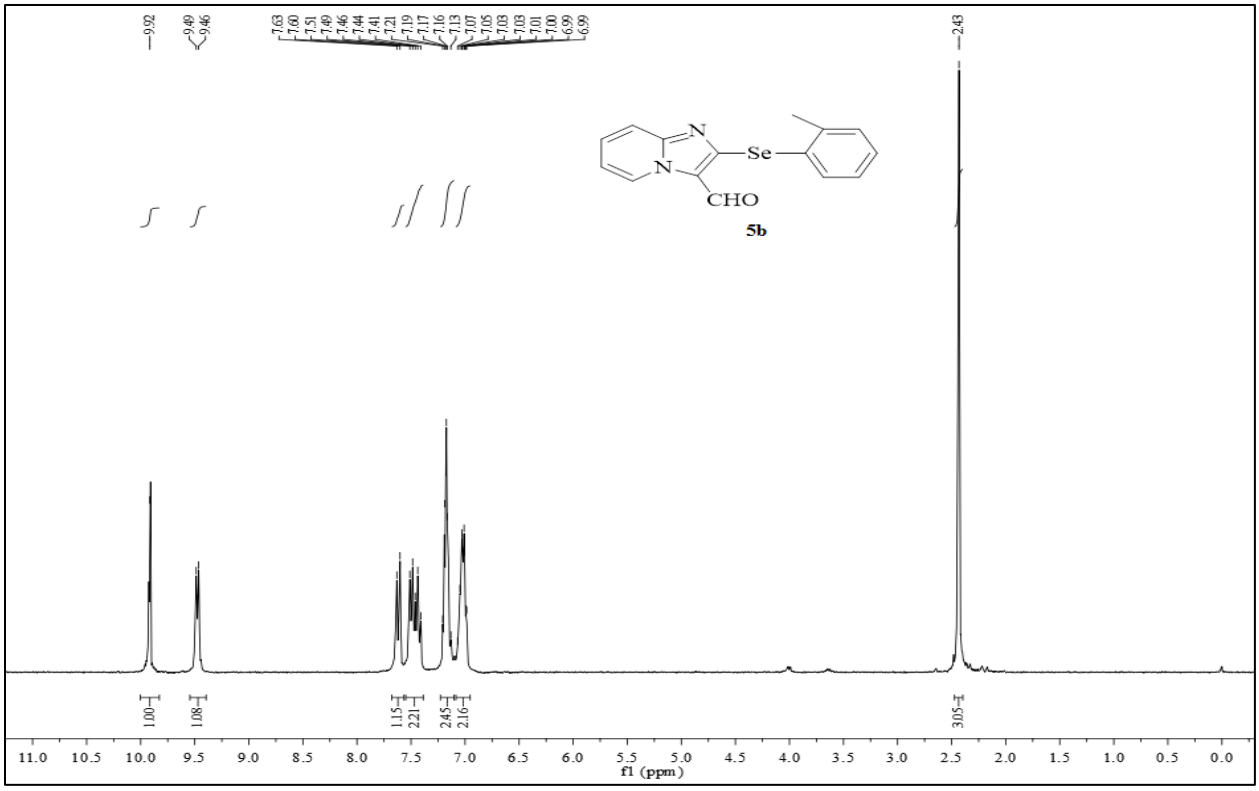


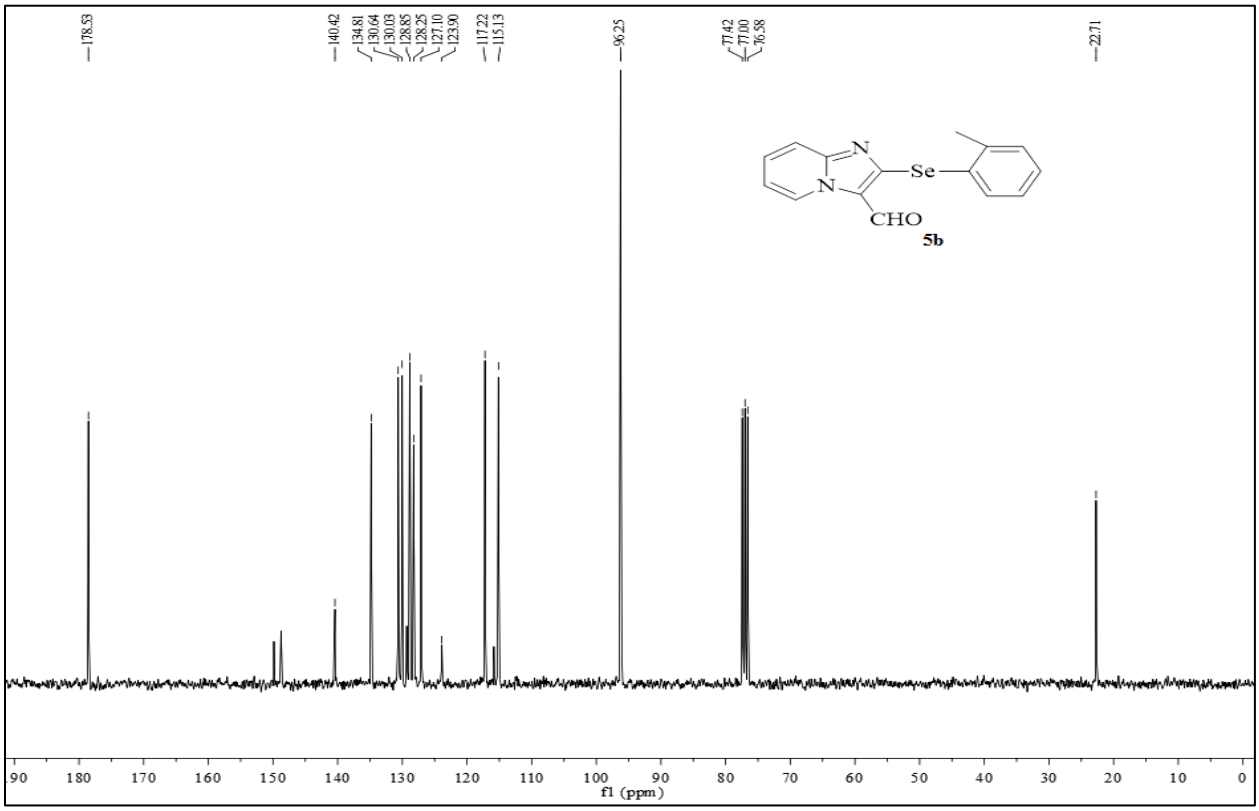


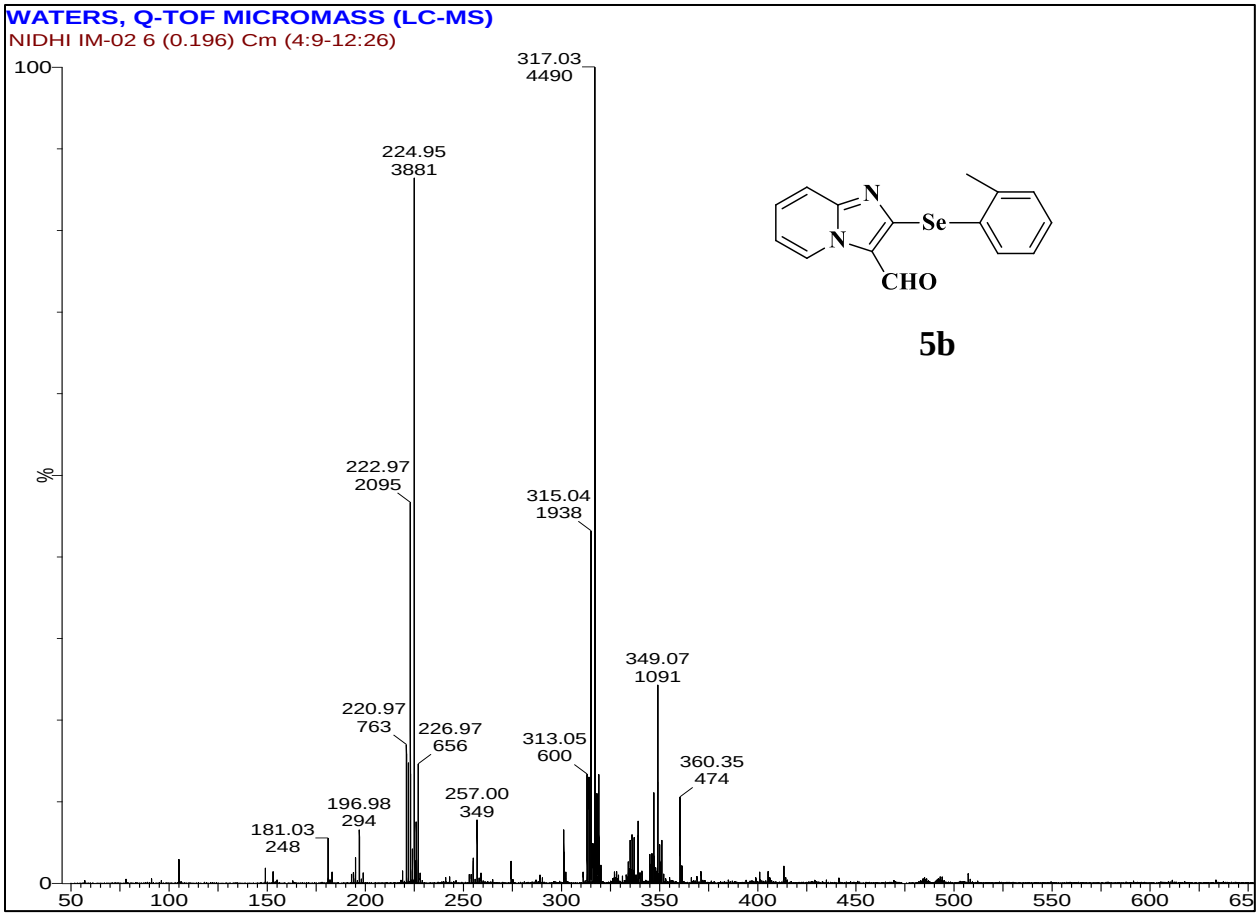

WATERS, Q-TOF MICROMASS (LC-MS)
SANJEEV SKM-1 17 (0.191) Cm (9:30)
100
%
0
303.0
26607
301.0
16144
299.1
5505
335.1
5426
333.1
2261
413.4
2048
225.0
1312
181.1
1104
100
150
200
250
300
350
400
450
500
550
N
N
Se
CHO

5a

^{1}H, ^{13}C-NMR of 2-(o-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5b)



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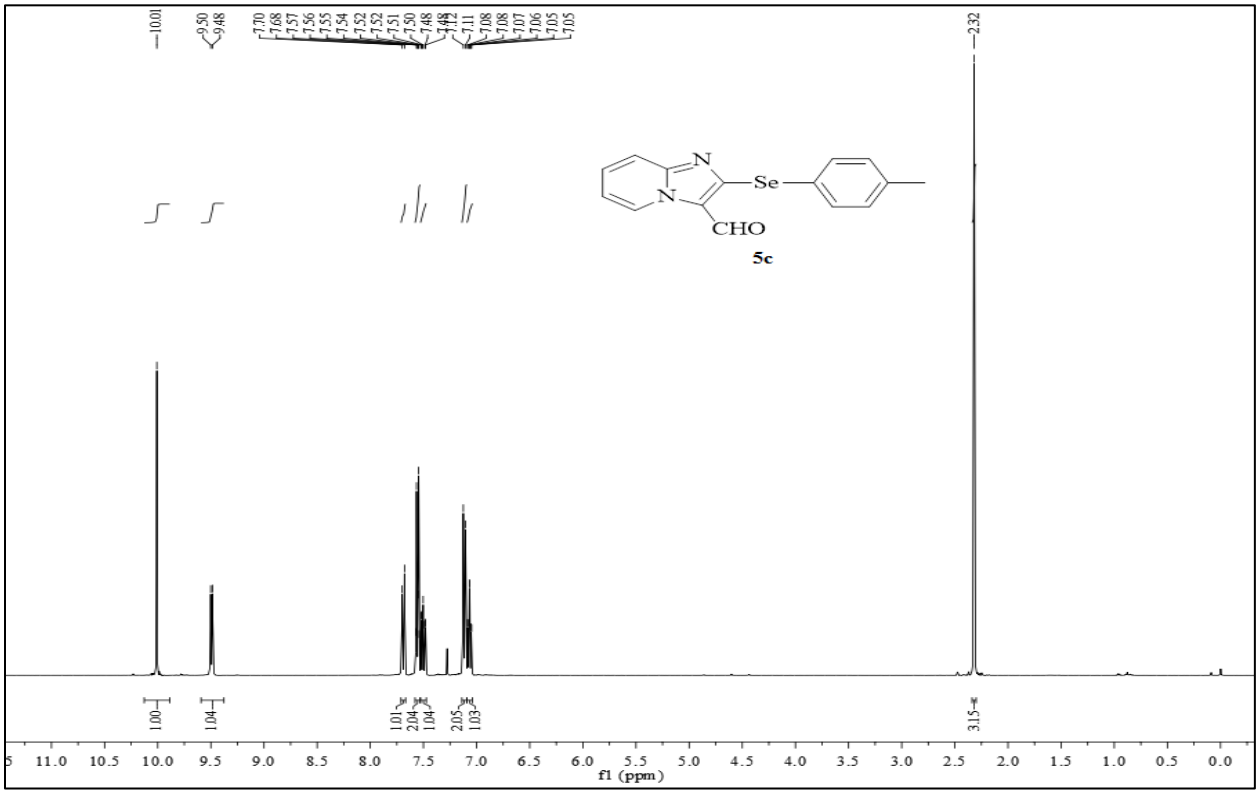
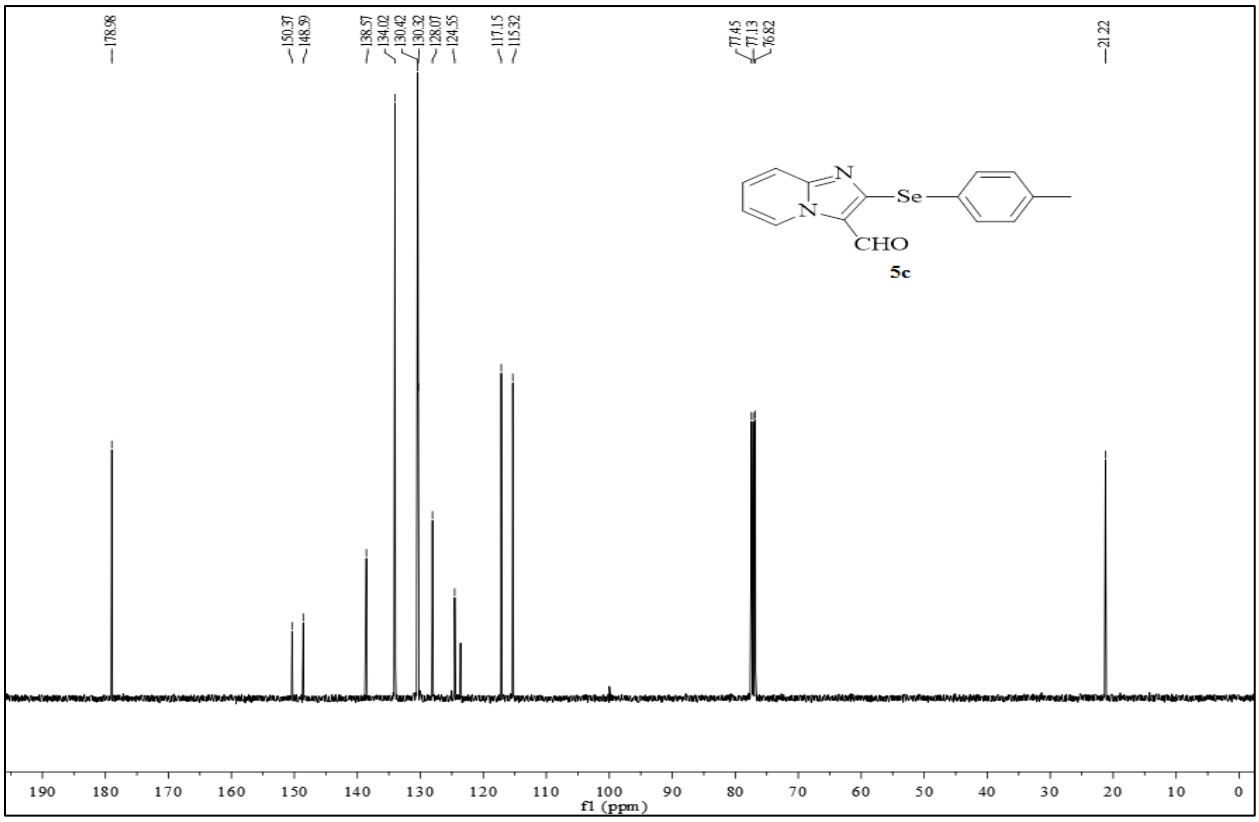
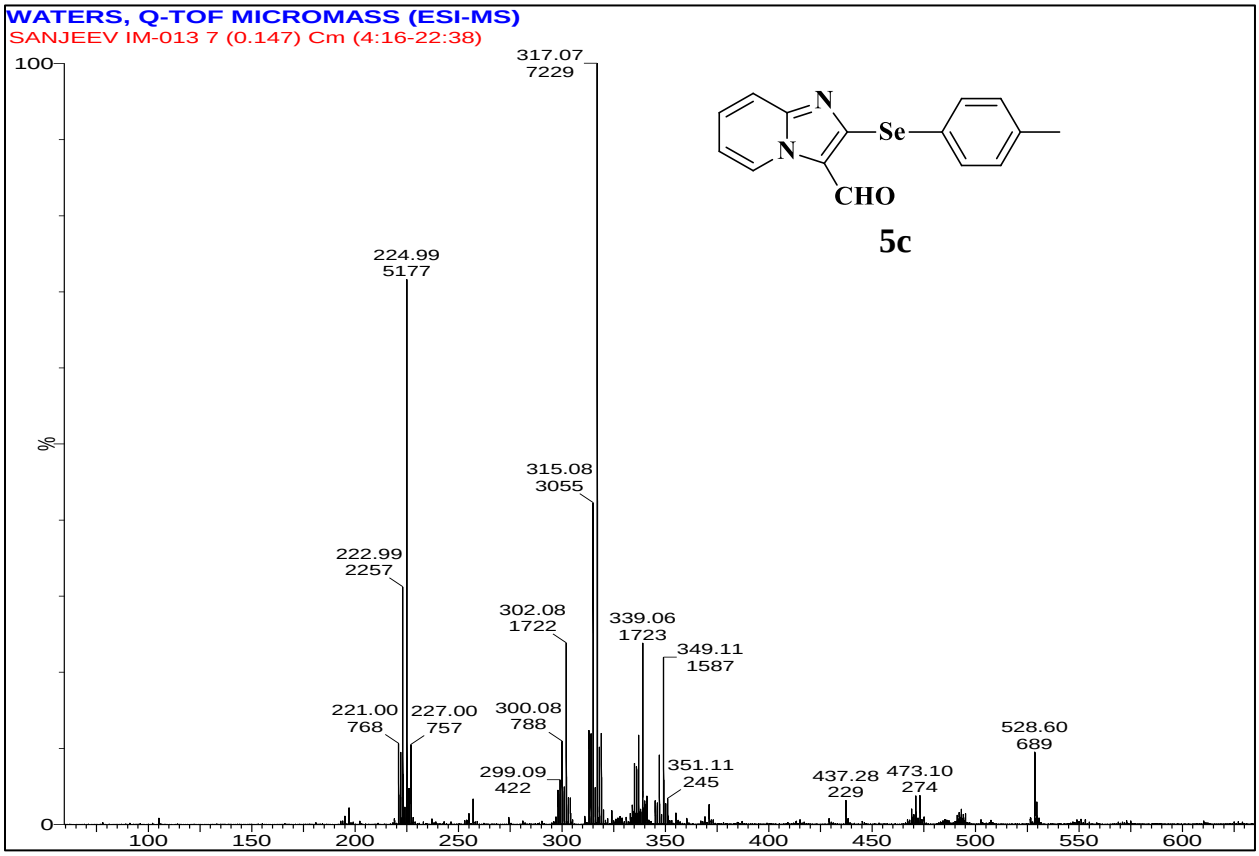
NIDHI IM-02 6 (0.196) Cm (4:9-12:26)
100
%
0
317.03
4490
224.95
3881
222.97
2095
315.04
1938
349.07
1091
220.97
763
226.97
656
313.05
600
360.35
474
257.00
349
196.98
294
181.03
248
50
100
150
200
250
300
350
400
450
500
550
600
65
N
Se
N
CHO

5b

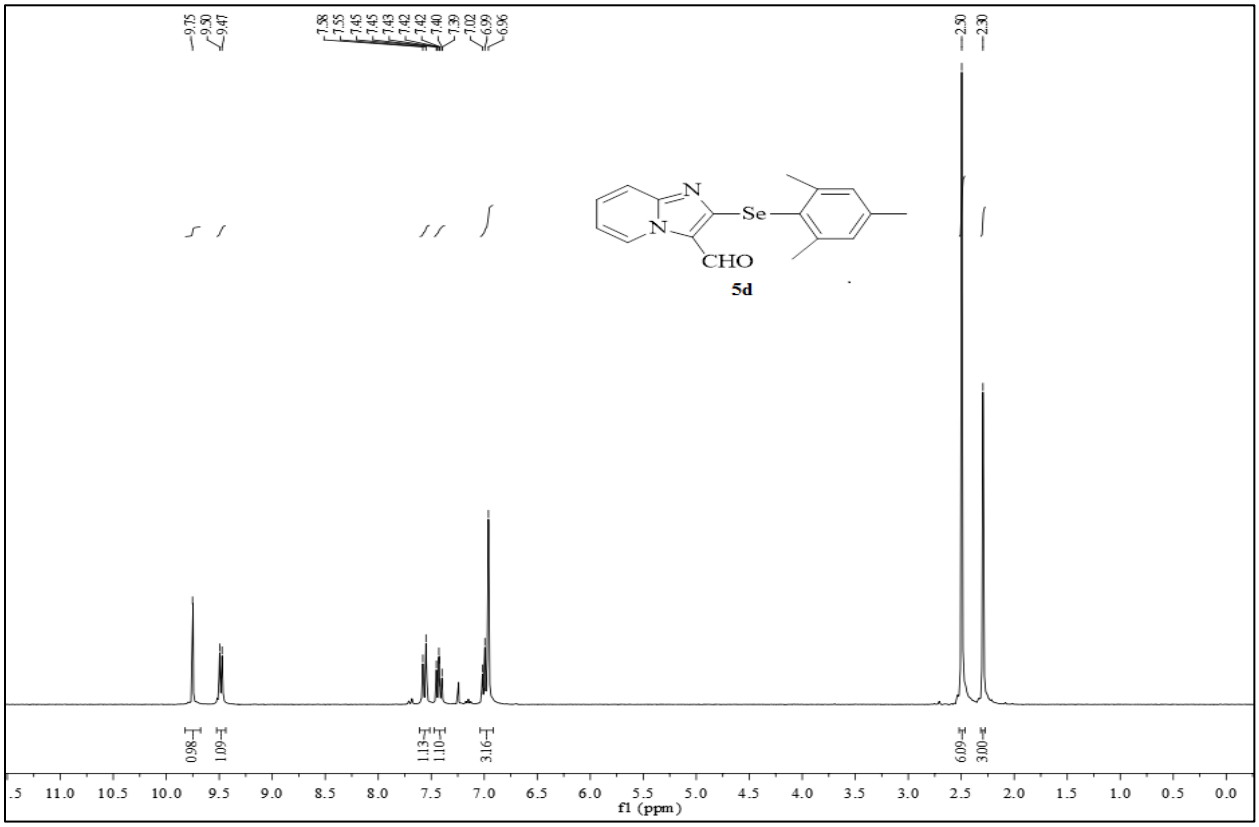
^{1}H, ^{13}C-NMR of 2-(p-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5c)

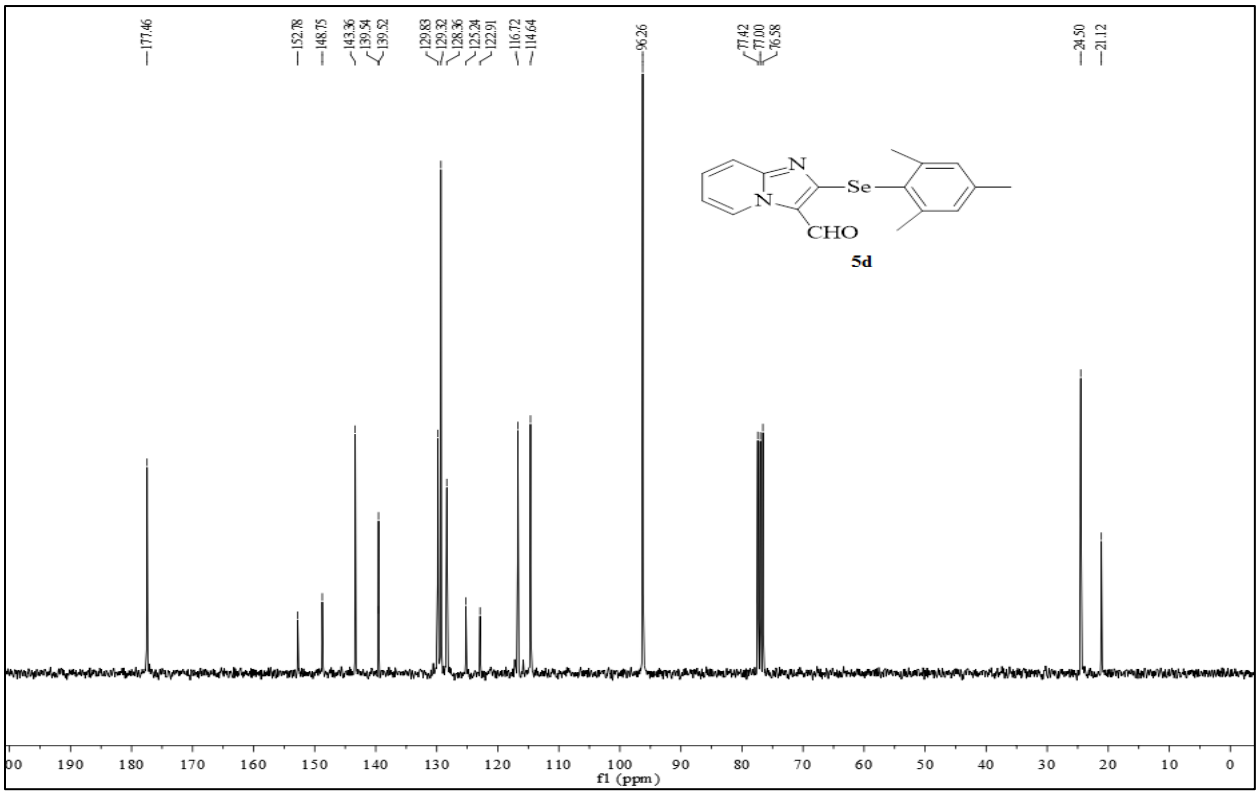


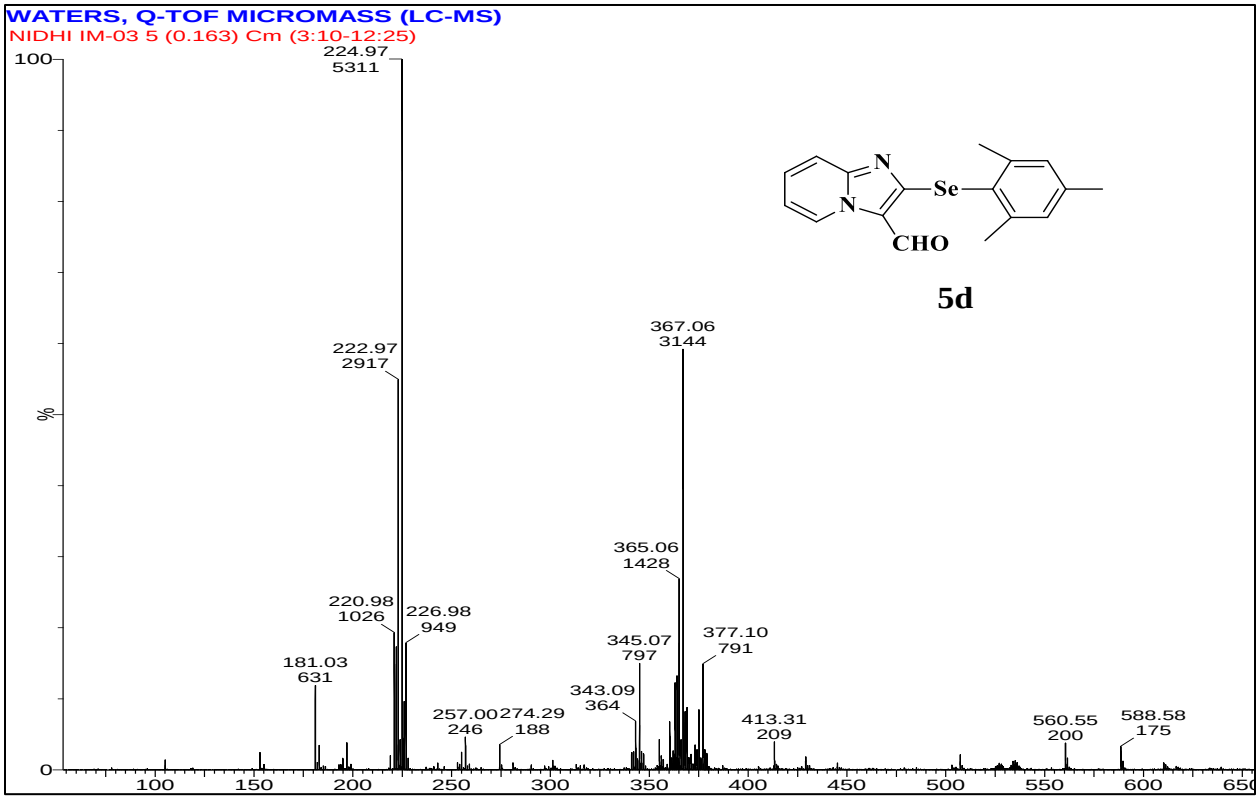



WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-013 7 (0.147) Cm (4:16-22:38)
100
%
0
317.07
7229
224.99
5177
315.08
3055
222.99
2257
302.08
1722
339.06
1723
349.11
1587
221.00
768
227.00
757
300.08
788
299.09
422
351.11
245
437.28
229
473.10
274
528.60
689
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
CHO
5c

^{1}H, ^{13}C-NMR of 2-(mesitylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5d)

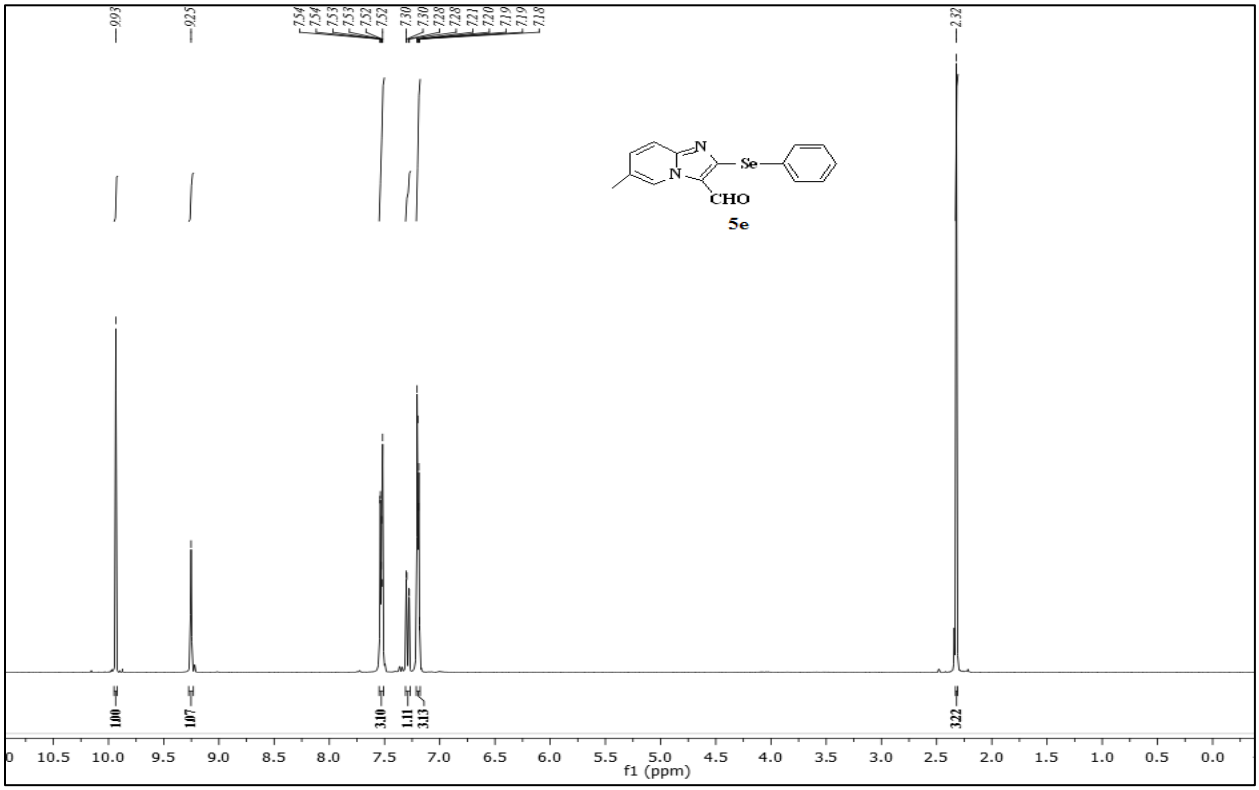


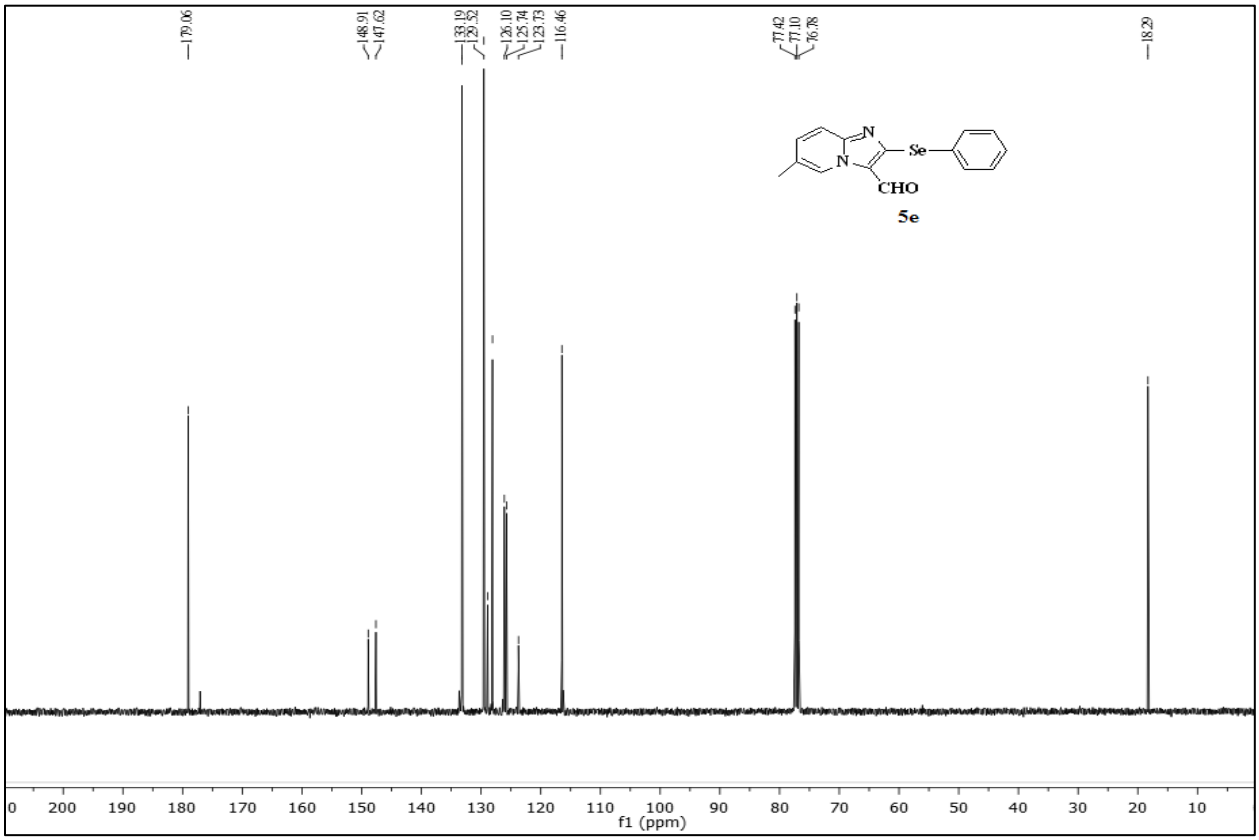


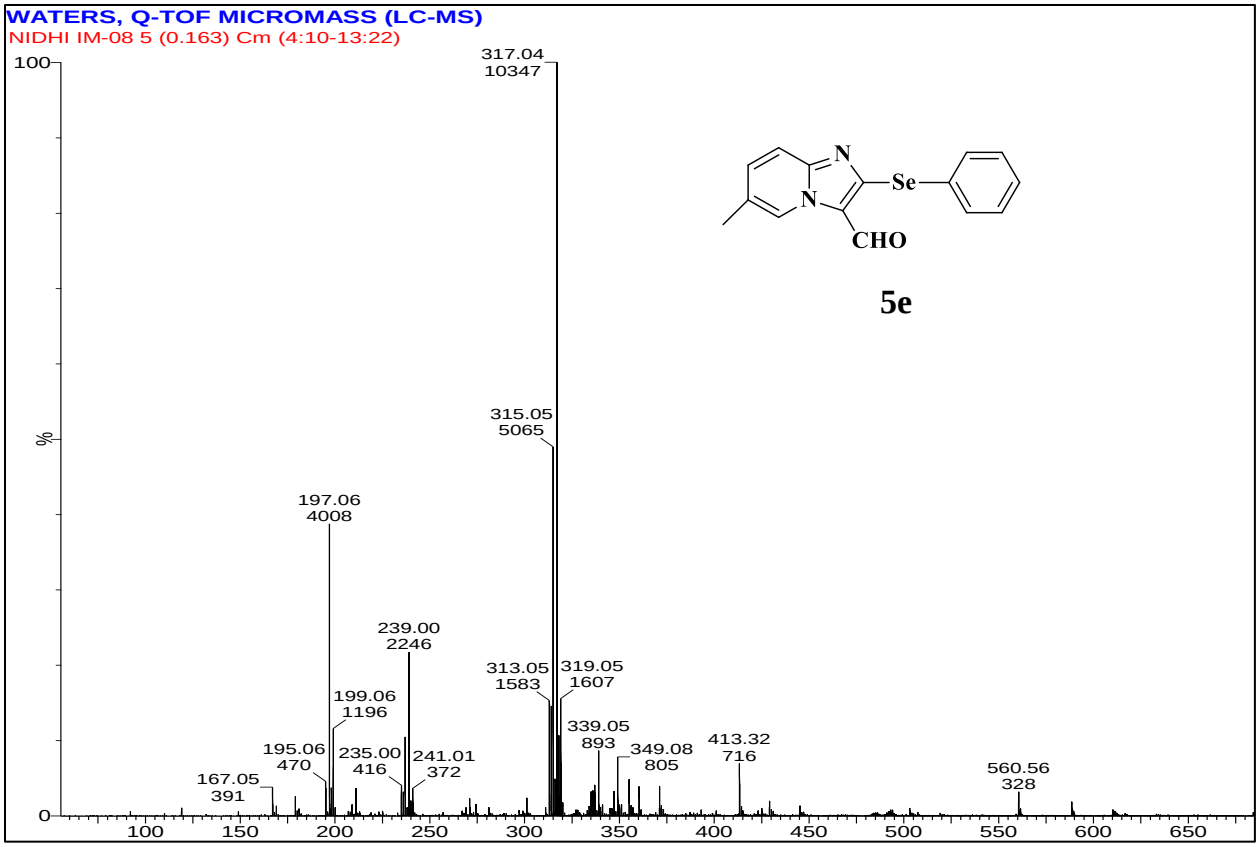

WATERS, Q-TOF MICROMASS (LC-MS)
NIDHI IM-03 5 (0.163) Cm (3:10-12:25)
100
%
0
224.97
5311
222.97
2917
367.06
3144
365.06
1428
220.98
1026
226.98
949
345.07
797
377.10
791
181.03
631
343.09
364
257.00
246
274.29
188
413.31
209
560.55
200
588.58
175
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
CHO

5d

^{1}H, ^{13}C-NMR of 6-methyl-2-(phenylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5e)

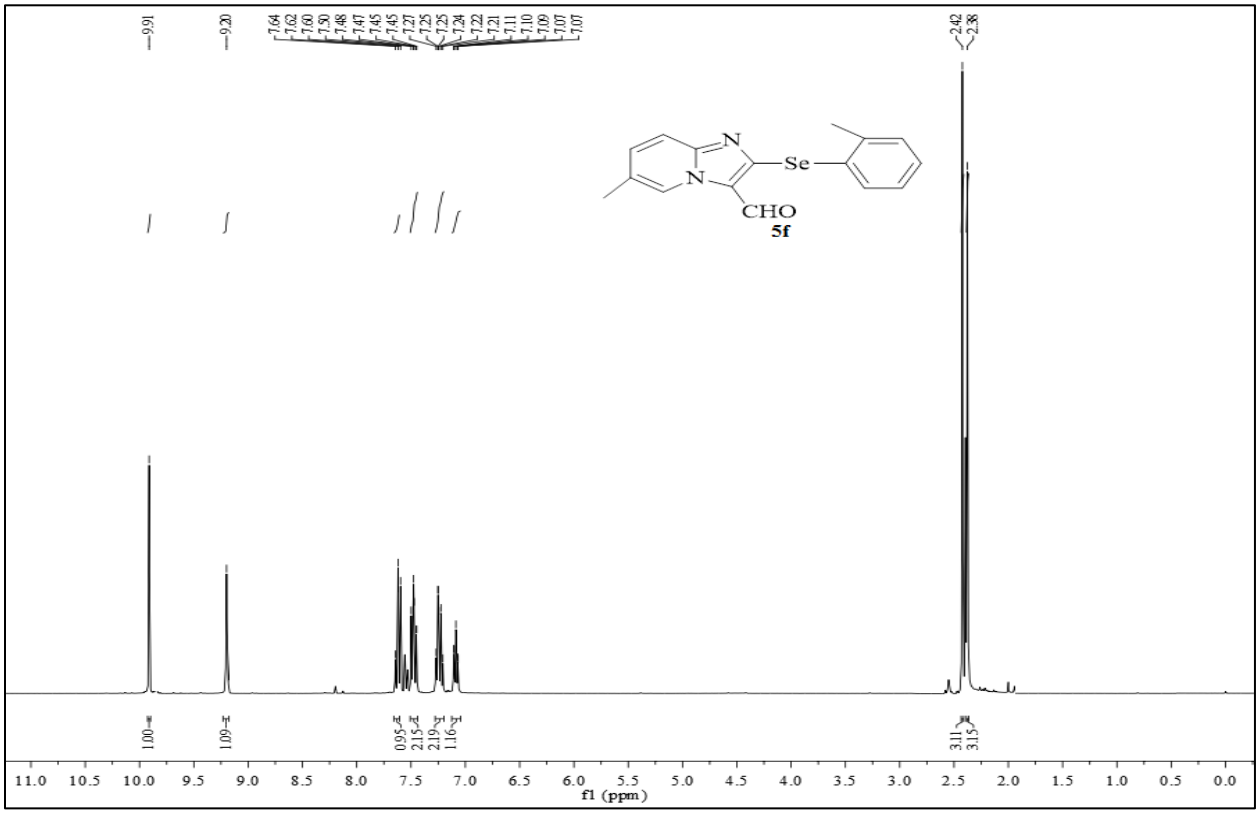


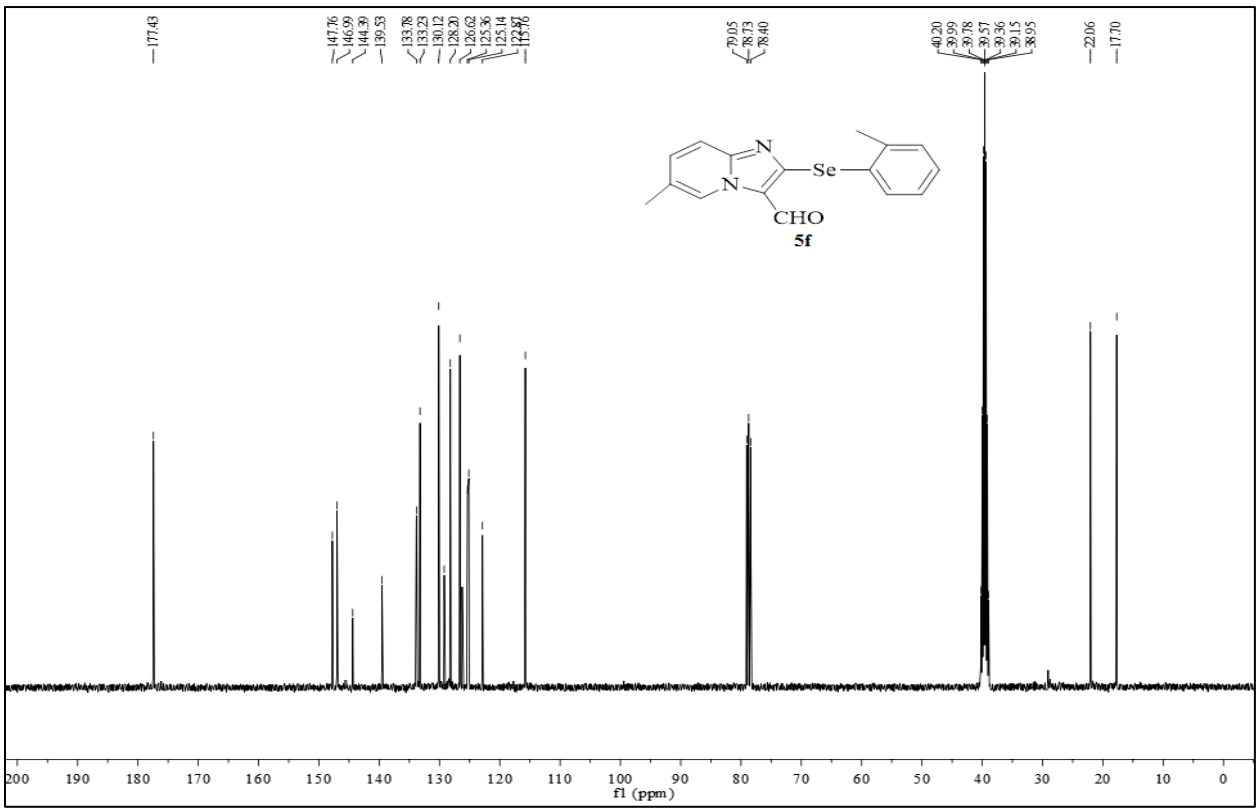


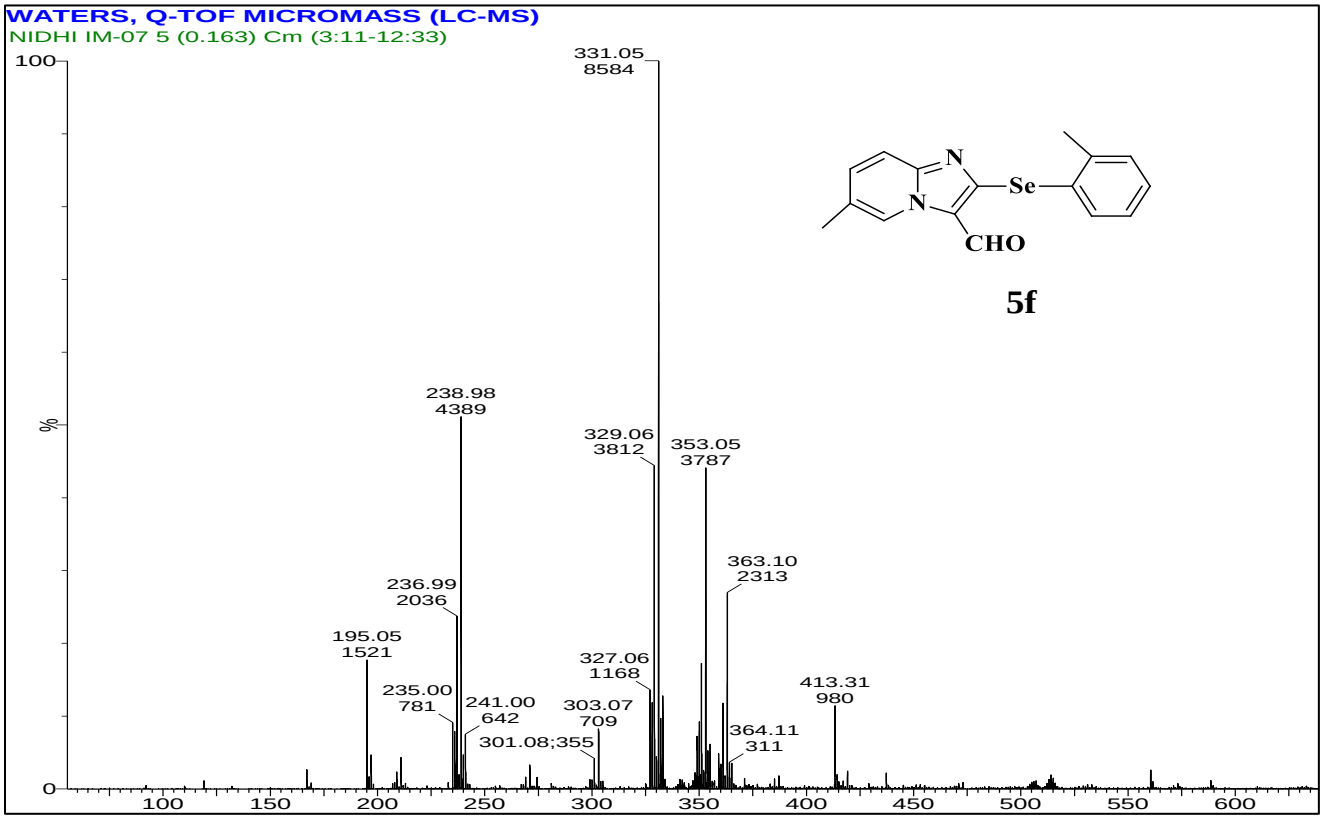

WATERS, Q-TOF MICROMASS (LC-MS)
NIDHI IM-08 5 (0.163) Cm (4:10-13:22)
100
%
0
317.04
10347
315.05
5065
197.06
4008
239.00
2246
313.05
1583
319.05
1607
199.06
1196
339.05
893
195.06
470
235.00
416
241.01
372
349.08
805
413.32
716
167.05
391
560.56
328
100
150
200
250
300
350
400
450
500
550
600
650
N
N
Se
CHO

5e

^{1}H, ^{13}C-NMR of 6-methyl-2-(o-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5f)

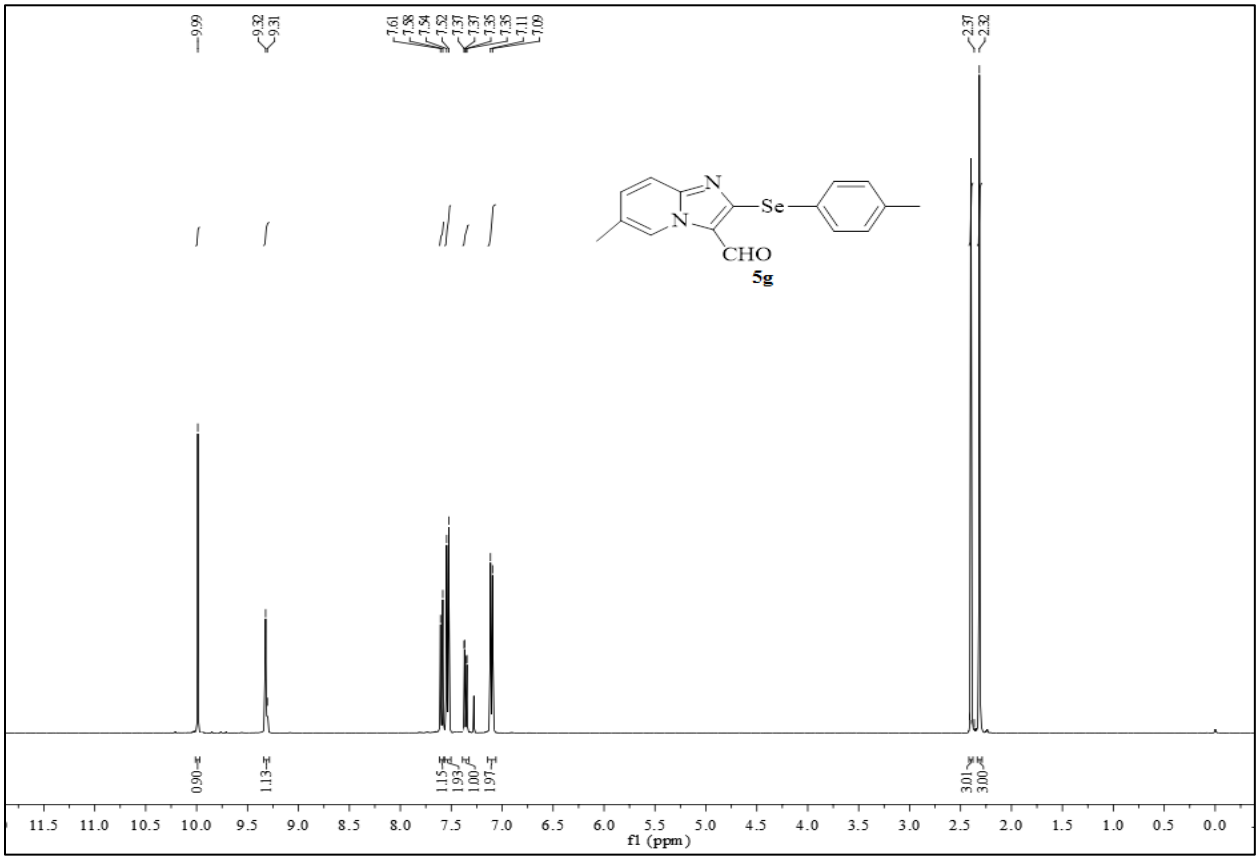


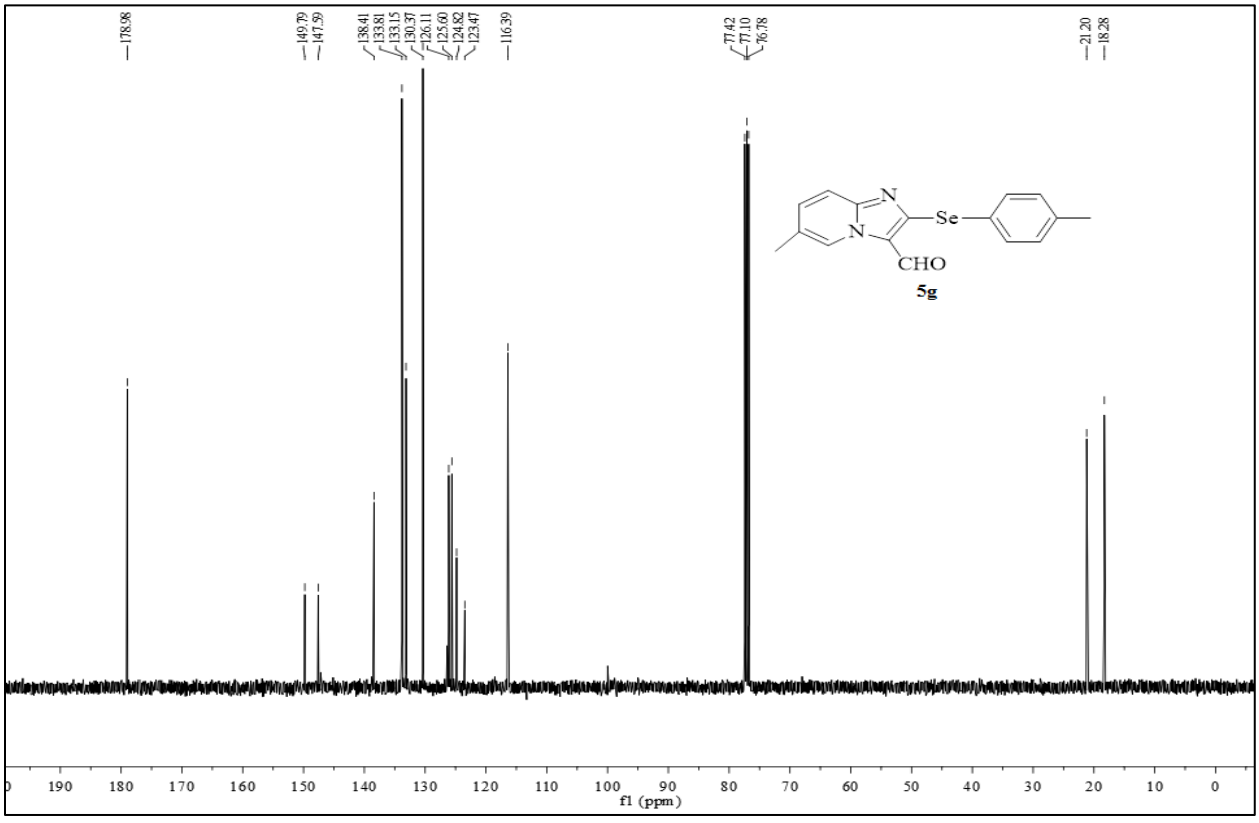


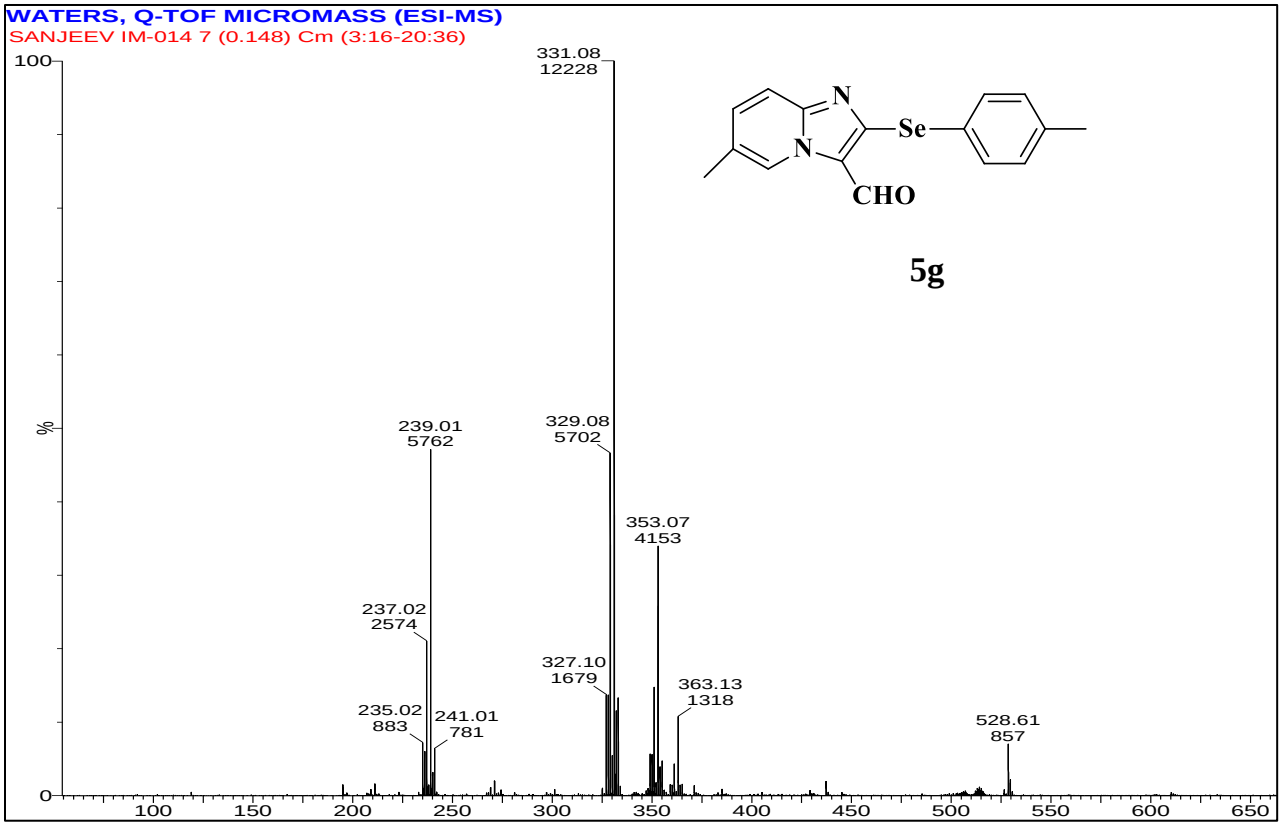

WATERS, Q-TOF MICROMASS (LC-MS)
NIDHI IM-07 5 (0.163) Cm (3:11-12:33)
100
%
0
331.05
8584
238.98
4389
329.06
3812
353.05
3787
363.10
2313
236.99
2036
195.05
1521
327.06
1168
413.31
980
235.00
781
241.00
642
303.07
709
301.08;355
364.11
311
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
CHO

5f

^{1}H, ^{13}C-NMR of6-methyl-2-(p-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde 5g

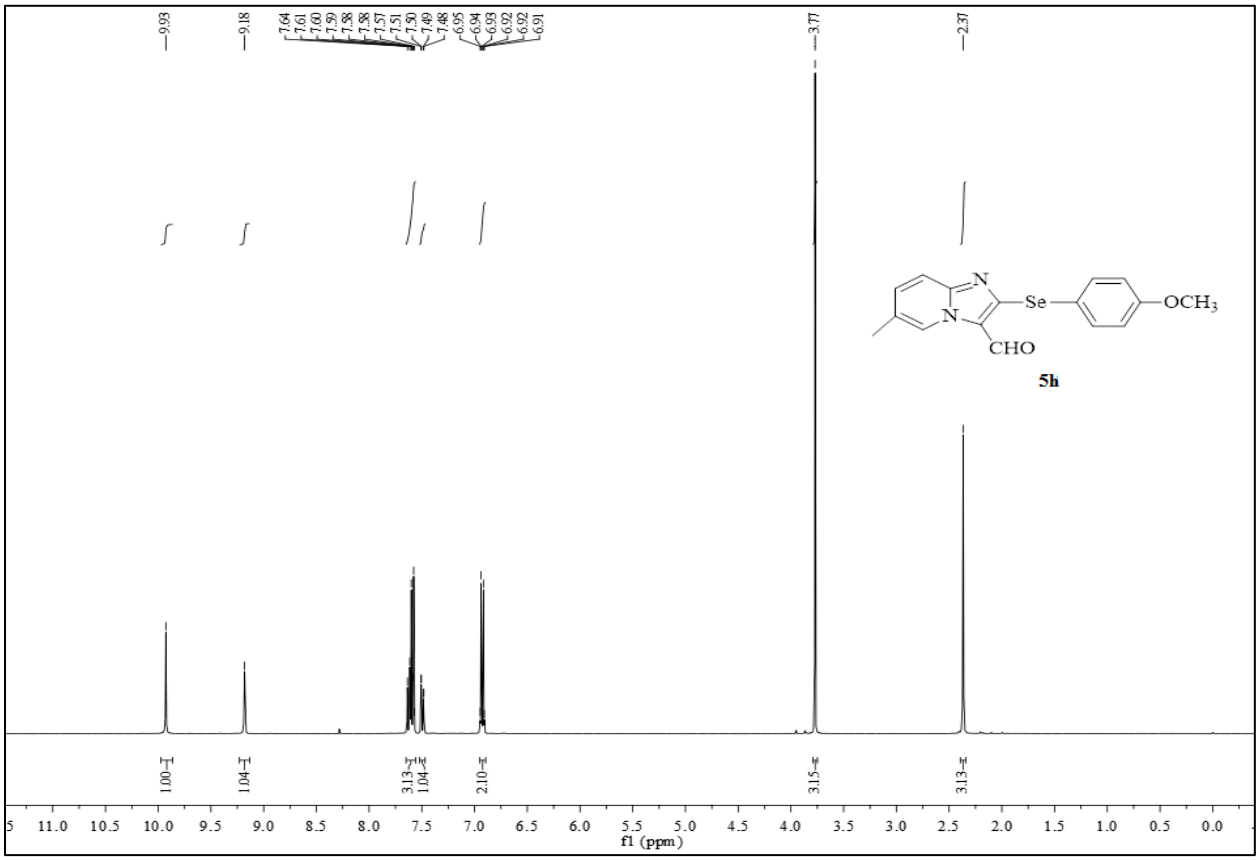


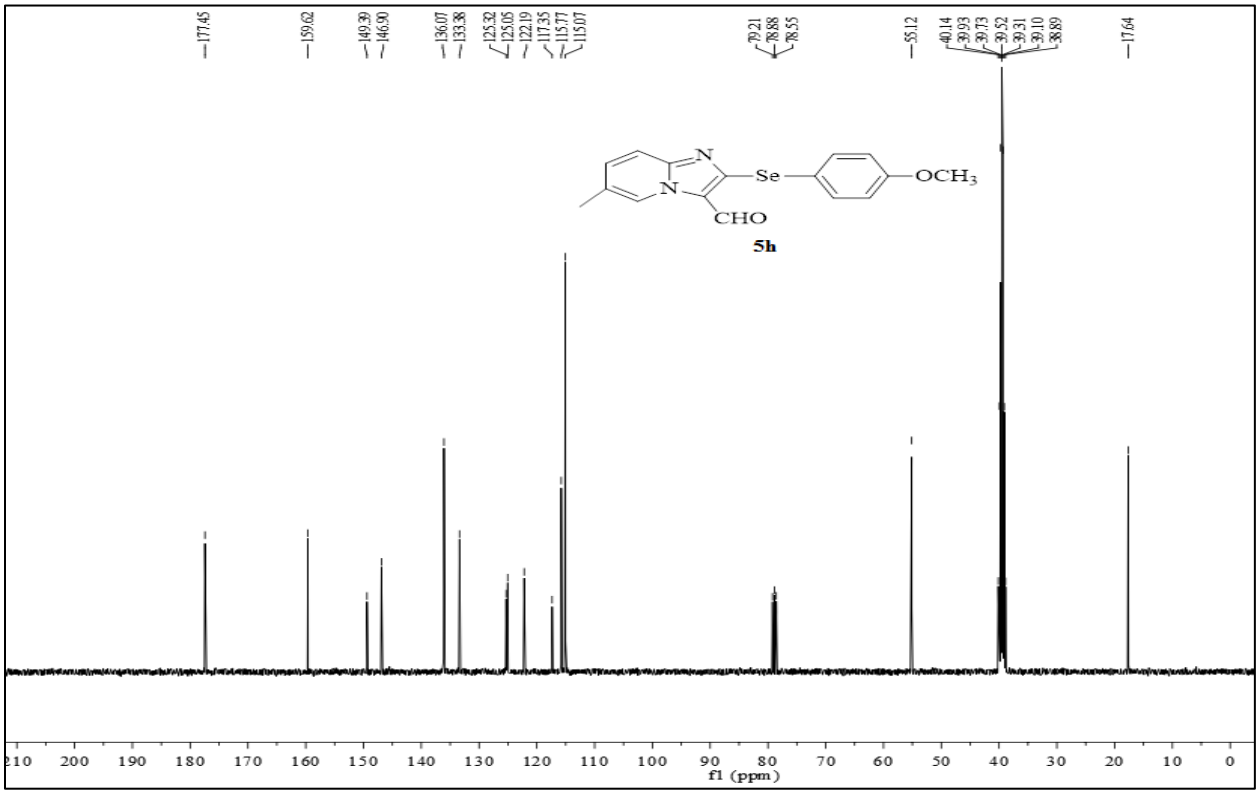


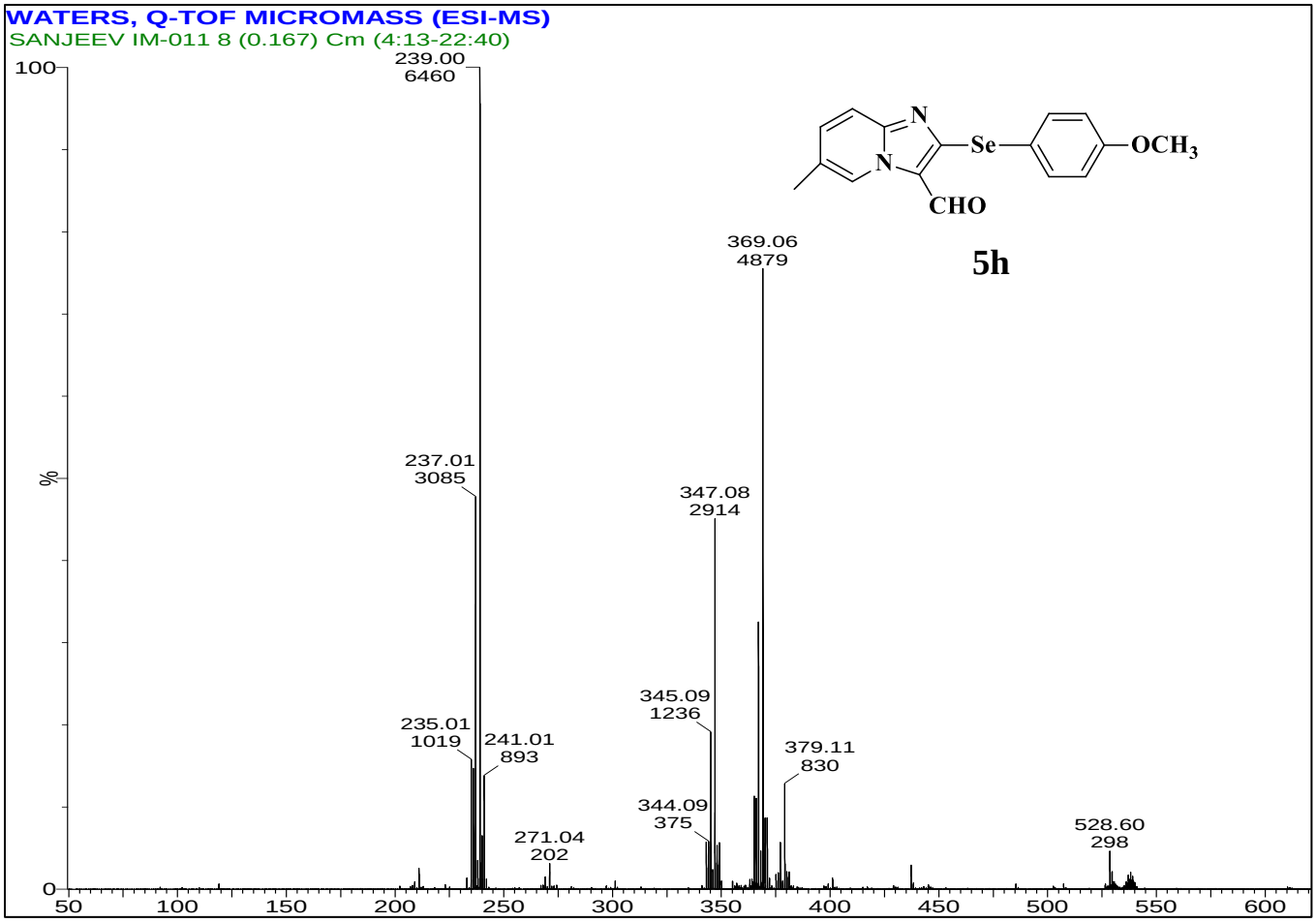

WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-014 7 (0.148) Cm (3:16-20:36)
100
%
0
331.08
12228
239.01
5762
329.08
5702
353.07
4153
237.02
2574
327.10
1679
363.13
1318
235.02
883
241.01
781
528.61
857
100
150
200
250
300
350
400
450
500
550
600
650
N
N
Se
CHO

5g

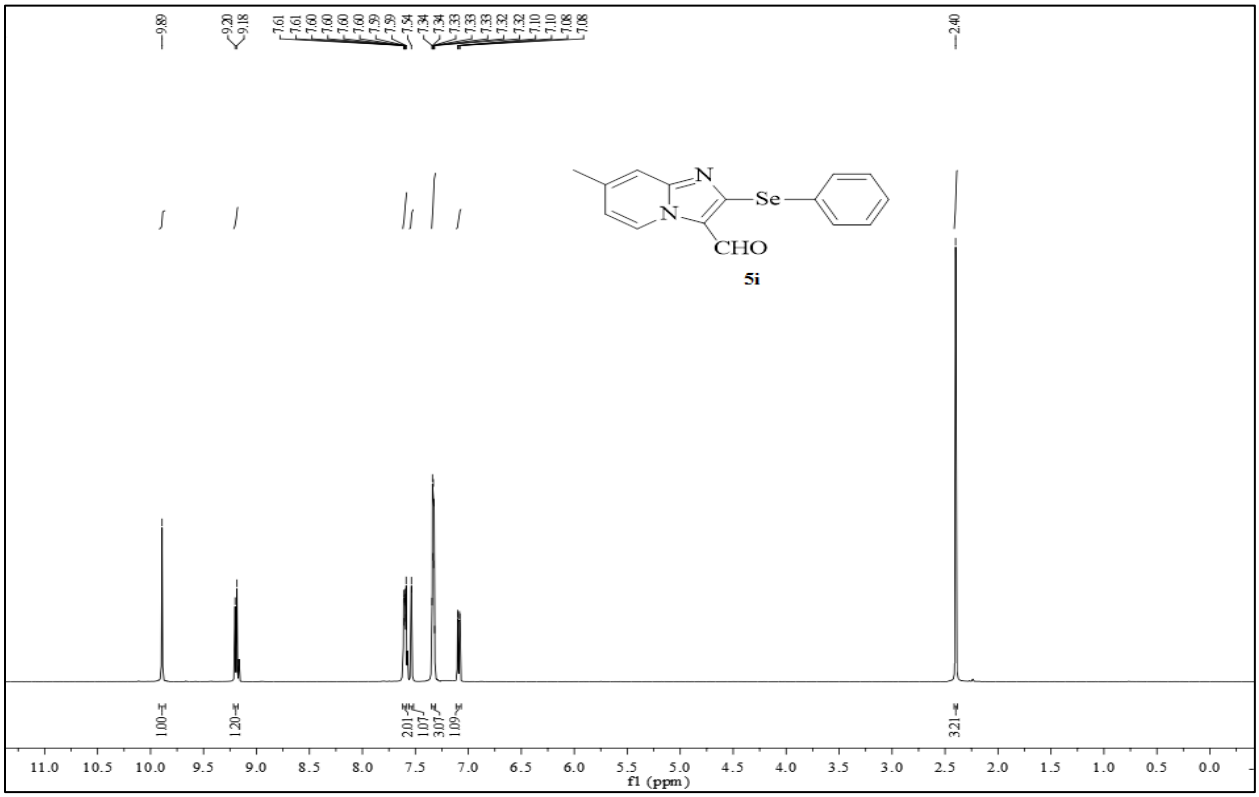
^{1}H, ^{13}C-NMR of2-((4-methoxyphenyl)selanyl)-6-methylimidazo[1,2-a]pyridine-3-carbaldehyde (5h)

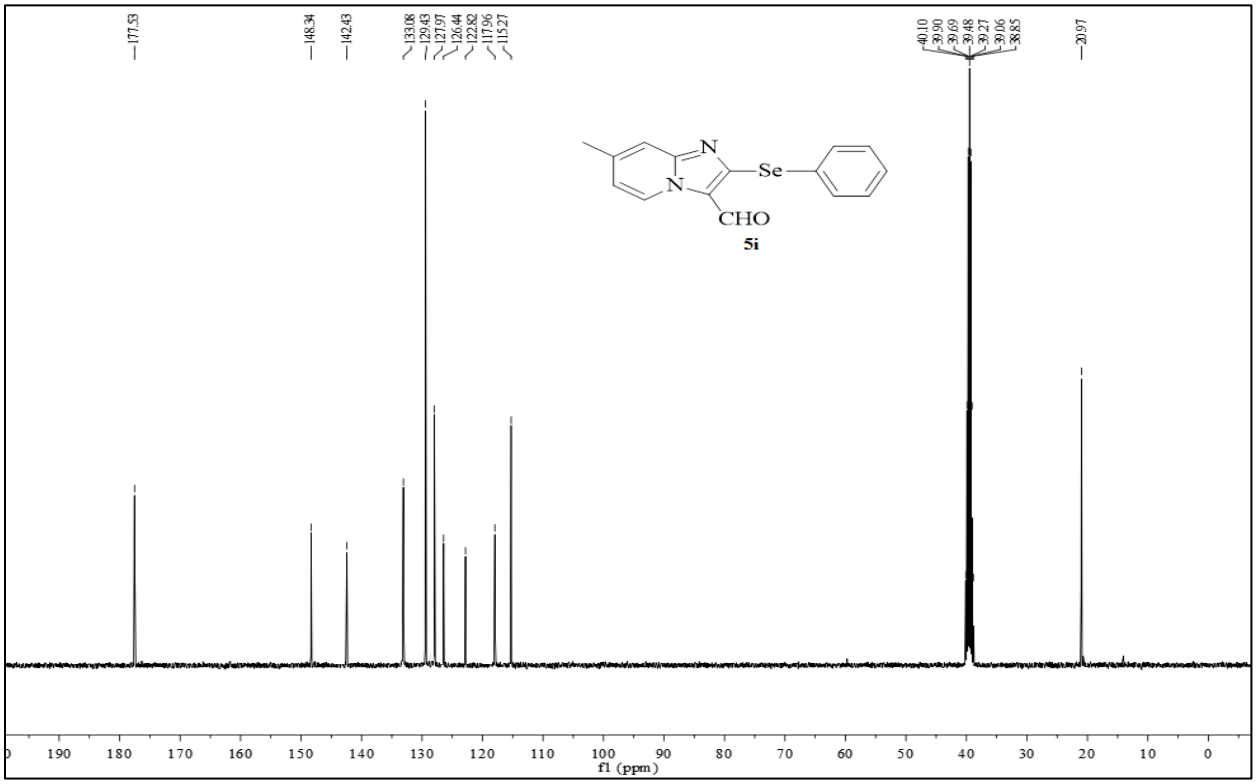


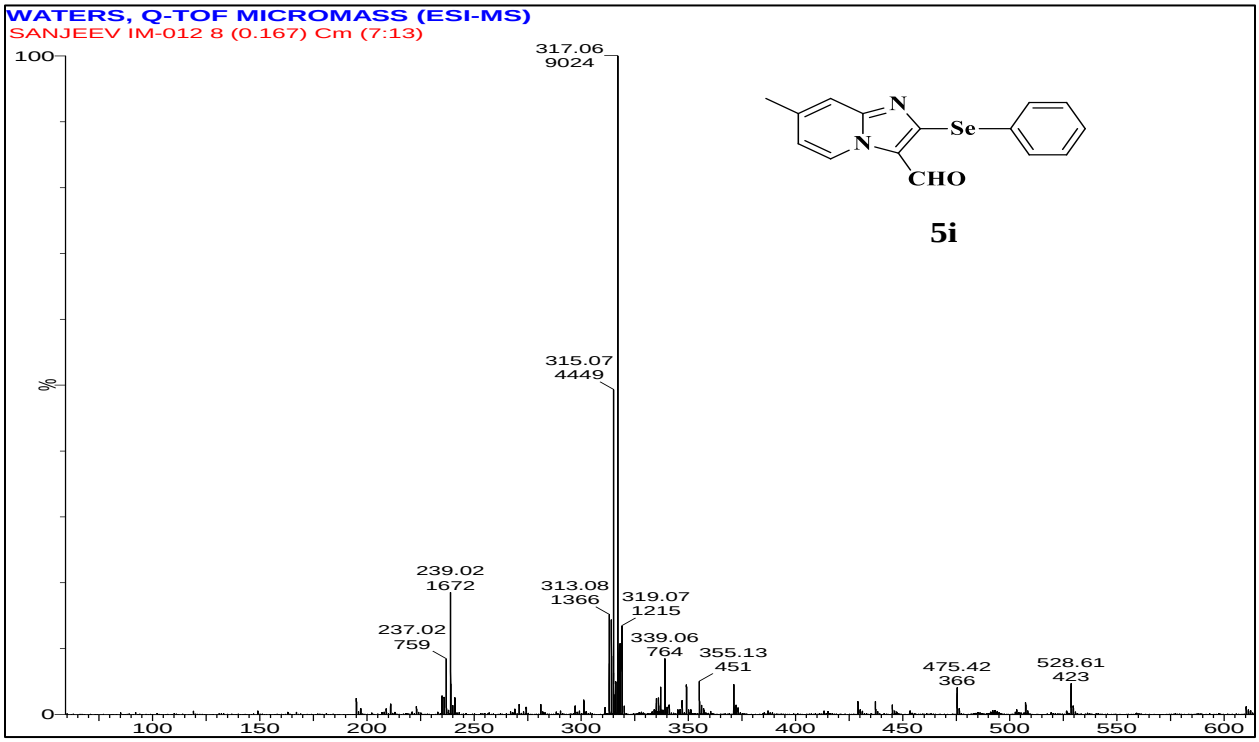



WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-011 8 (0.167) Cm (4:13-22:40)
100
%
0
239.00
6460
237.01
3085
235.01
1019
241.01
893
271.04
202
347.08
2914
345.09
1236
344.09
375
369.06
4879
379.11
830
528.60
298
50
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
OCH3
CHO
5h

^{1}H, ^{13}C-NMR of7-methyl-2-(phenylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde 5i

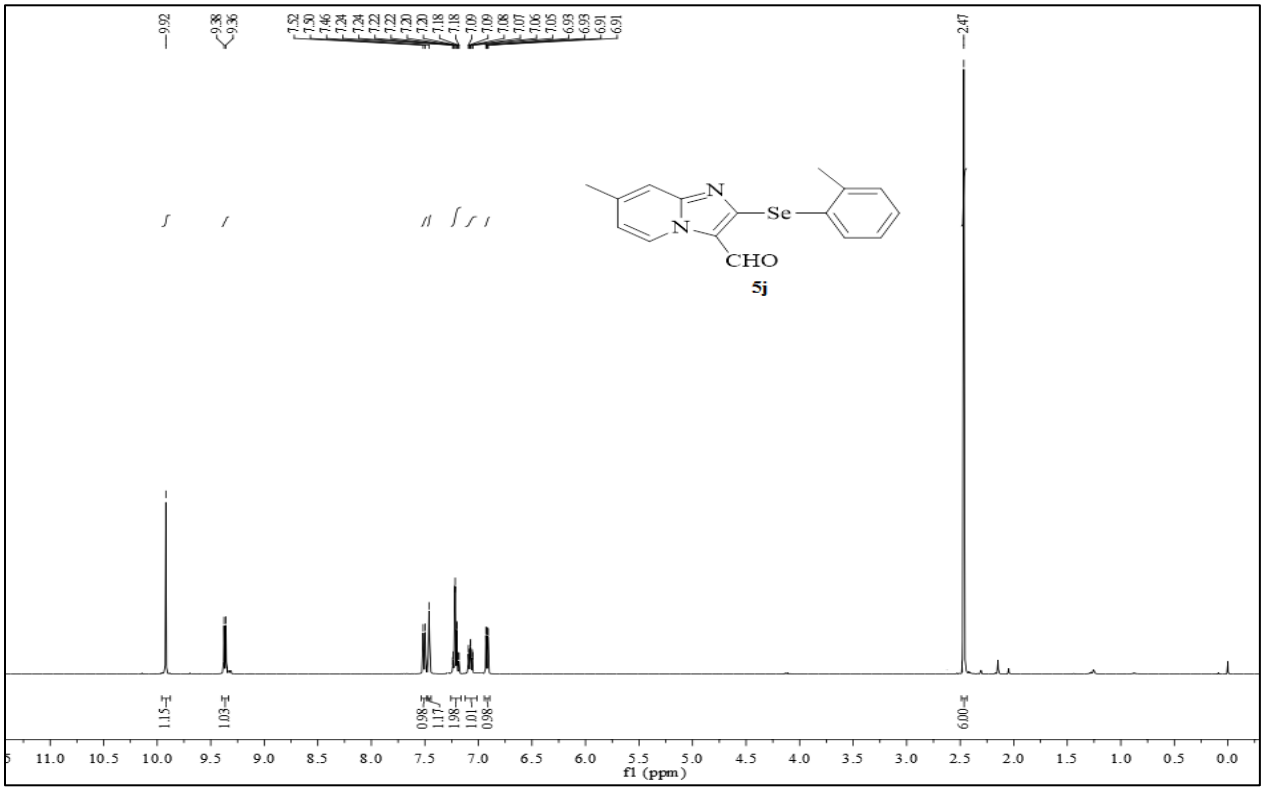


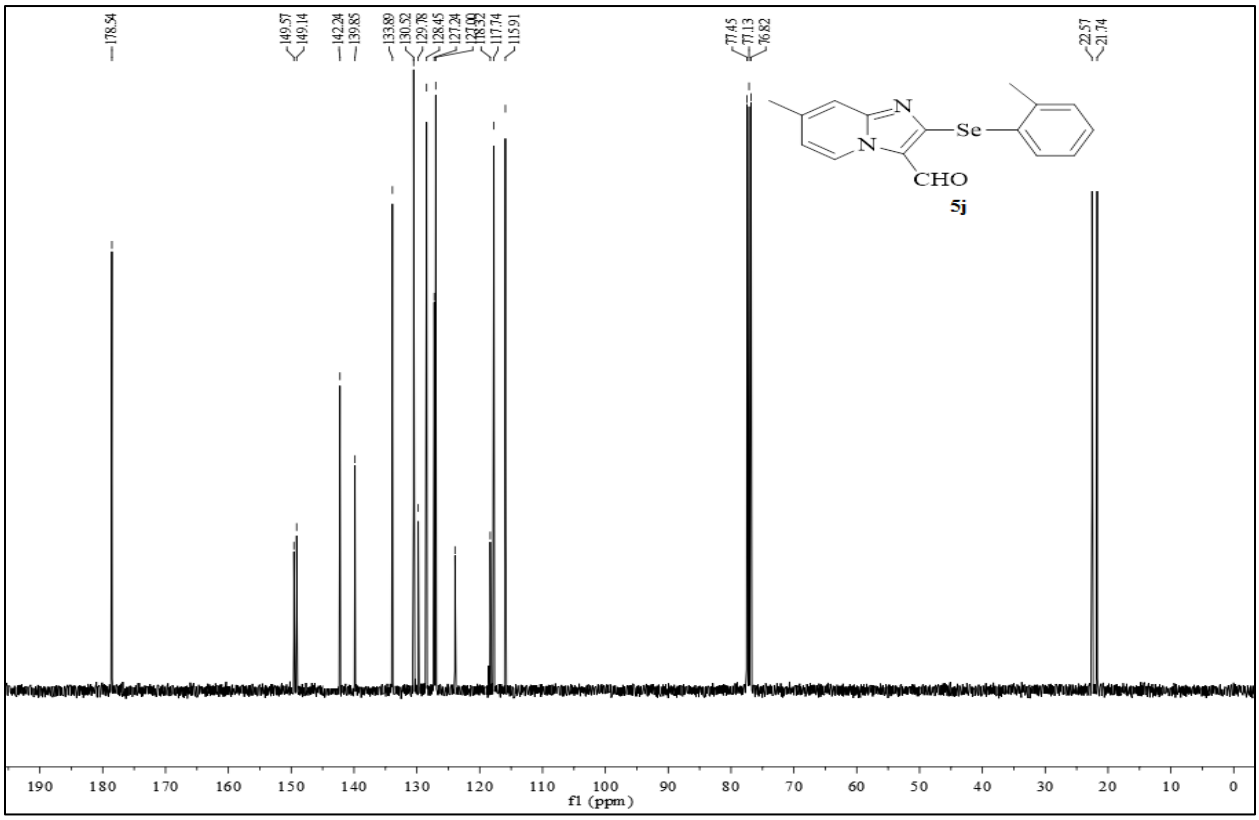


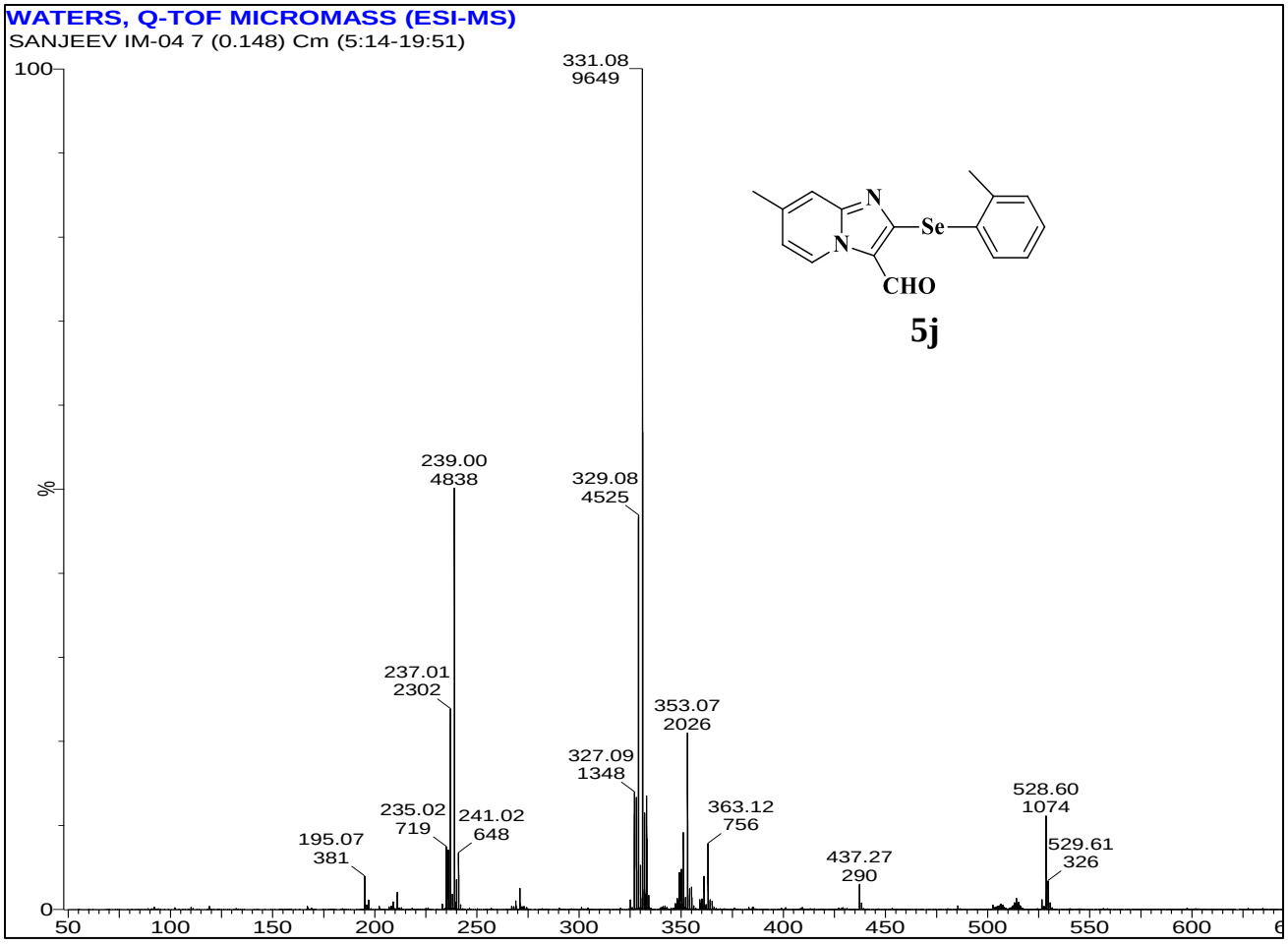

WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-012 8 (0.167) Cm (7:13)
100
%
0
317.06
9024
315.07
4449
239.02
1672
313.08
1366
319.07
1215
237.02
759
339.06
764
355.13
451
475.42
366
528.61
423
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
CHO

5i

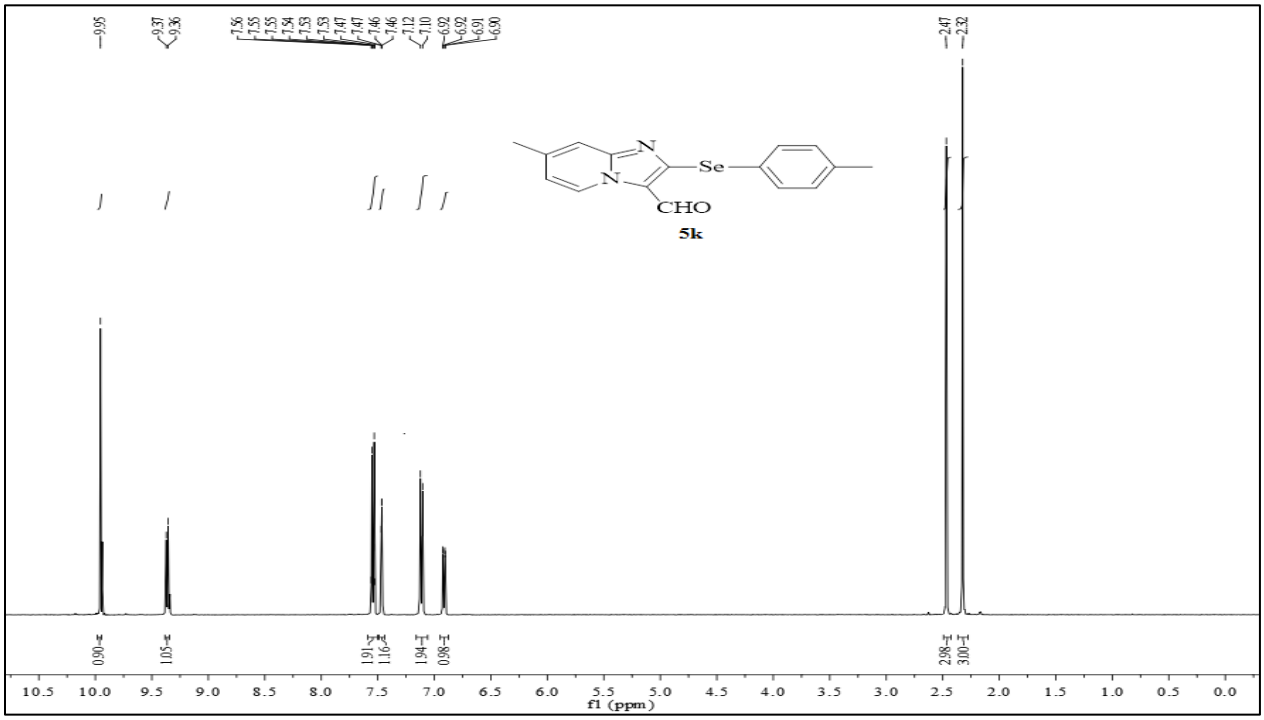
^{1}H, ^{13}C-NMR of 7-methyl-2-(o-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde 5j

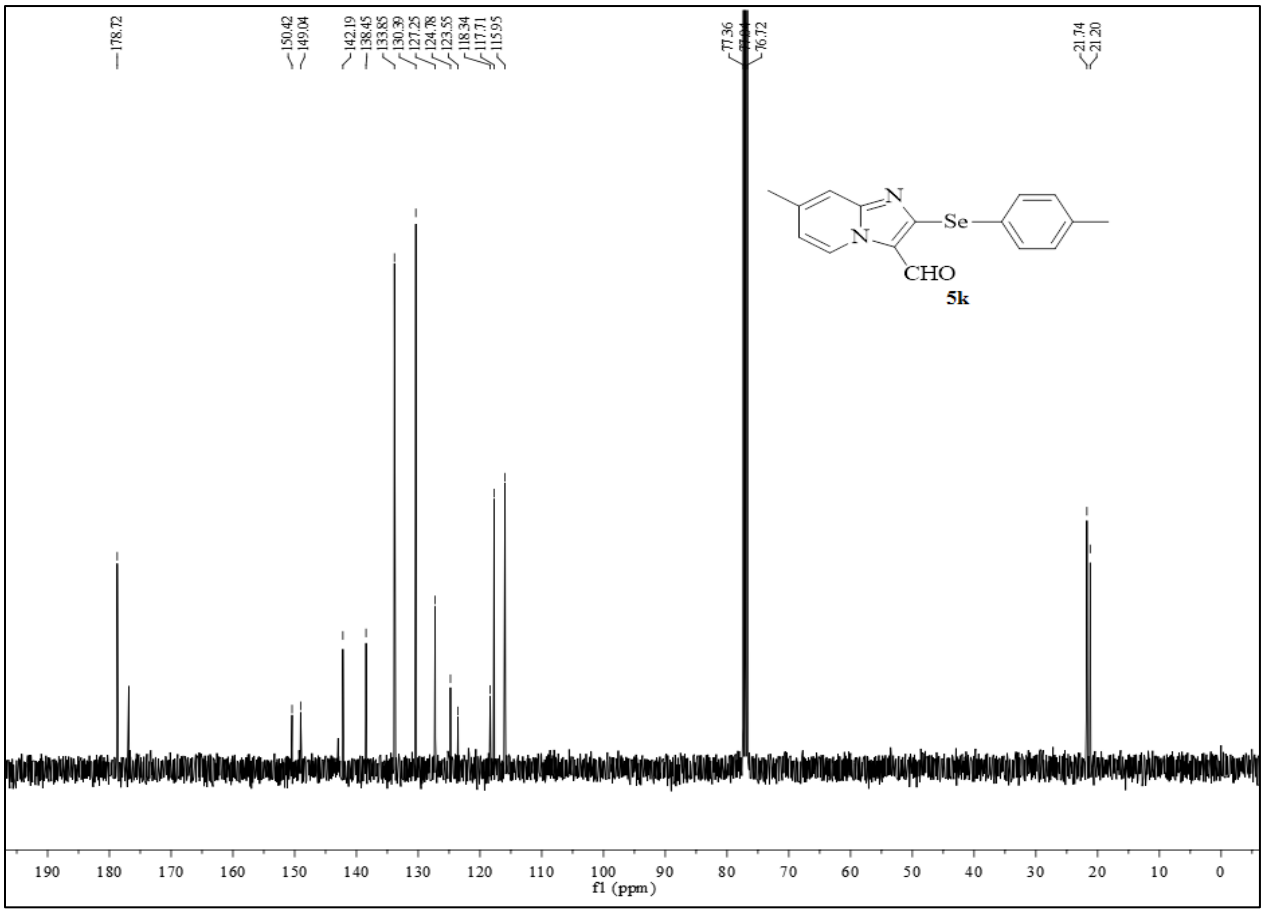


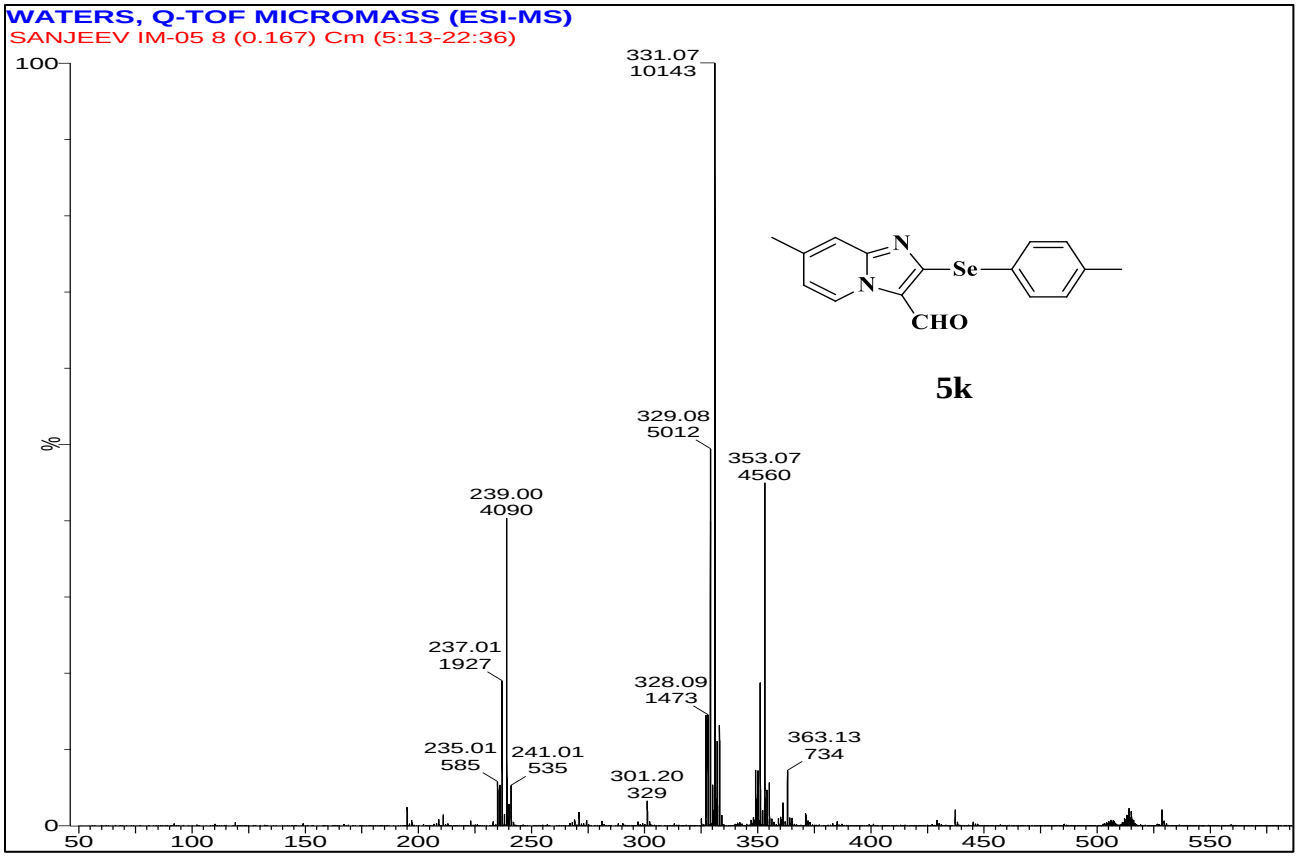



WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-04 7 (0.148) Cm (5:14-19:51)
100
%
0
331.08
9649
239.00
4838
329.08
4525
237.01
2302
353.07
2026
327.09
1348
235.02
719
241.02
648
363.12
756
195.07
381
437.27
290
528.60
1074
529.61
326
50
100
150
200
250
300
350
400
450
500
550
600
N
N
Se
CHO
5j

^{1}H, ^{13}C-NMR of 7-methyl-2-(p-tolylselanyl)imidazo[1,2-a]pyridine-3-carbaldehyde (5k)





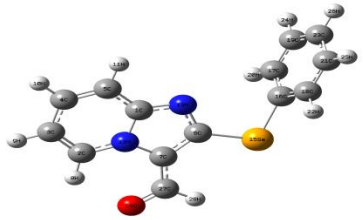
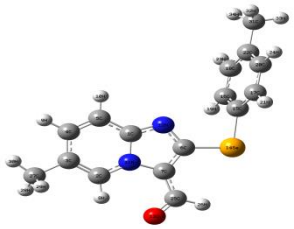
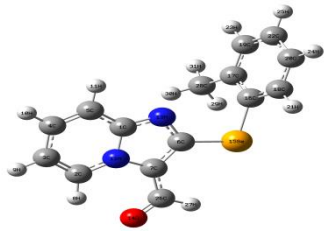
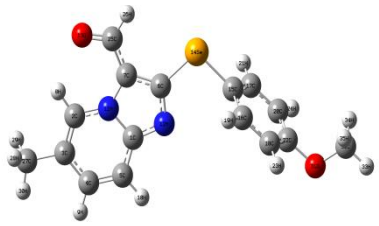
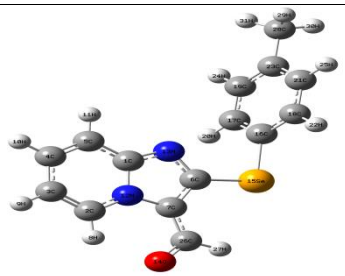
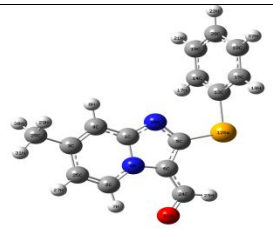
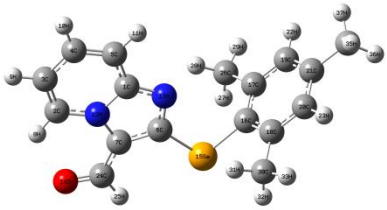
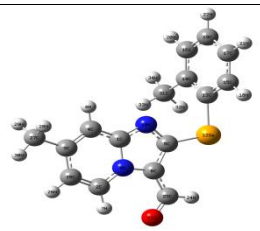
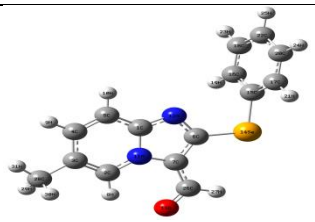
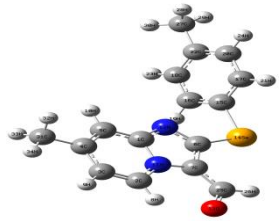
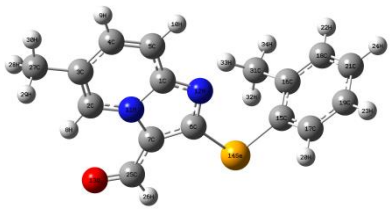

WATERS, Q-TOF MICROMASS (ESI-MS)
SANJEEV IM-05 8 (0.167) Cm (5:13-22:36)
100
%
0
331.07
10143
329.08
5012
353.07
4560
239.00
4090
237.01
1927
328.09
1473
363.13
734
235.01
585
241.01
535
301.20
329
50
100
150
200
250
300
350
400
450
500
550
N
N
Se
CHO

5k

Table S1. Crystal data and structure refinement for **5a**

Formula	$C_{14}H_{10}N_2OSe$
Mol. weight	301.2
Crystal system	Triclinic
Space group	P-1
a (Å)	5.5390(4)
b (Å)	8.1345(6)
c (Å)	13.8742(9)
α (°)	94.771(3)
β (°)	98.816(4)
γ (°)	93.294(4)
V (Å^3)	614.04(8)
Z	2
Temp in kelvin	298(2)
λ (Å)	0.71073
ρ calcd (g cm^{-3})	1.629
μ (mm^{-1})	3.05
Goodness of fit	1.015
θ range (°)	2.519–25.683
Total no. of rflns	18139
No. of unique rflns	2322
Observed data [I > 2σ(I)]	1880
R_{int}	0.0419
R_1, wR_2 [(I > 2σ(I)]	0.0303, 0.0663
R_1, wR_2 (all data)	0.0453, 0.0719

TABLE S2: Optimized structures of Compounds **5a-k** with DFT B3LYP 6-31G(d)

Compound	Optimized Structure	Compound	Optimized Structure
5a		**5g**	
5b		**5h**	
5c		**5i**	
5d		**5j**	
5e		**5k**	
5f			

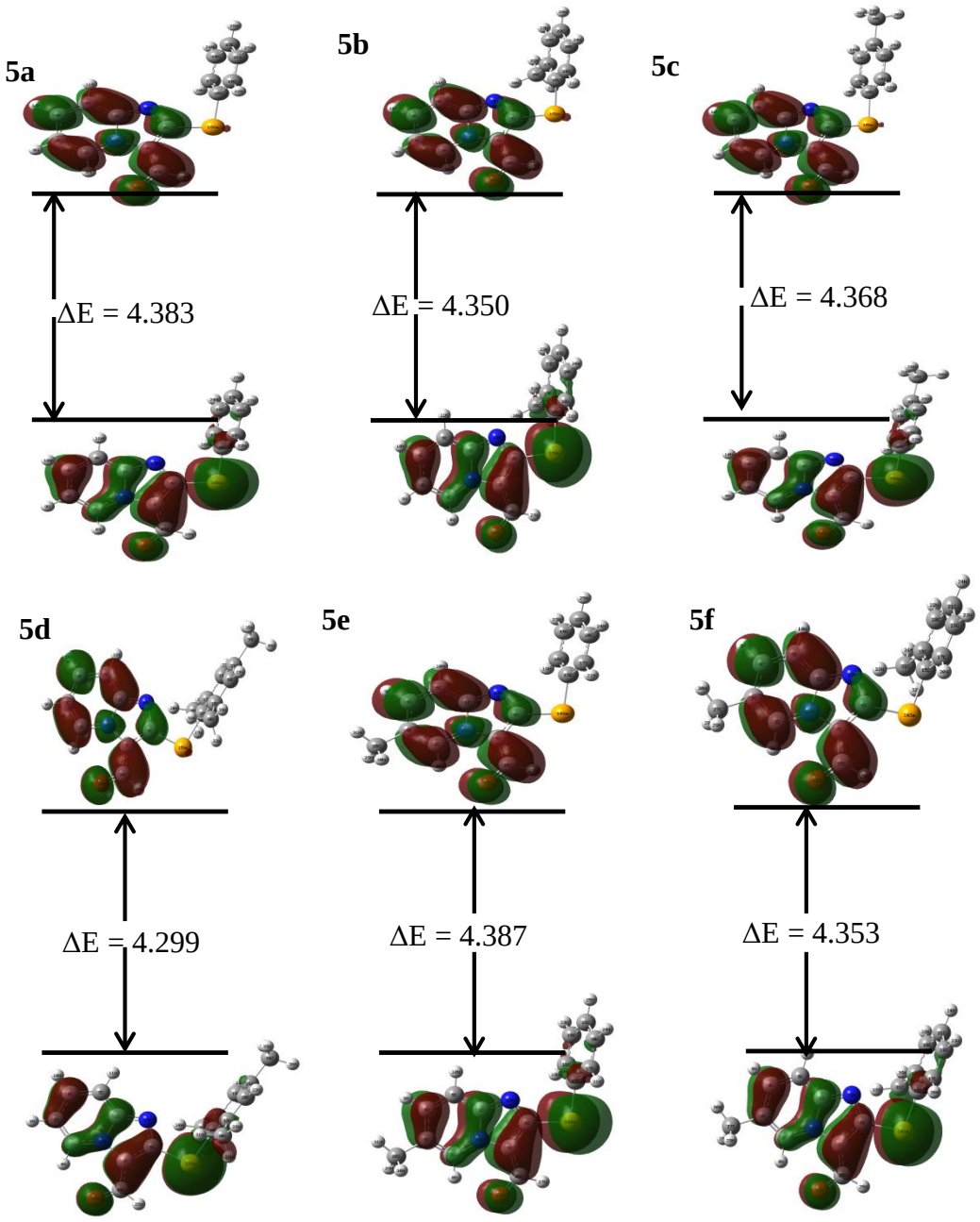


Figure 1. HOMO-LUMO diagram of compounds **5a-f**

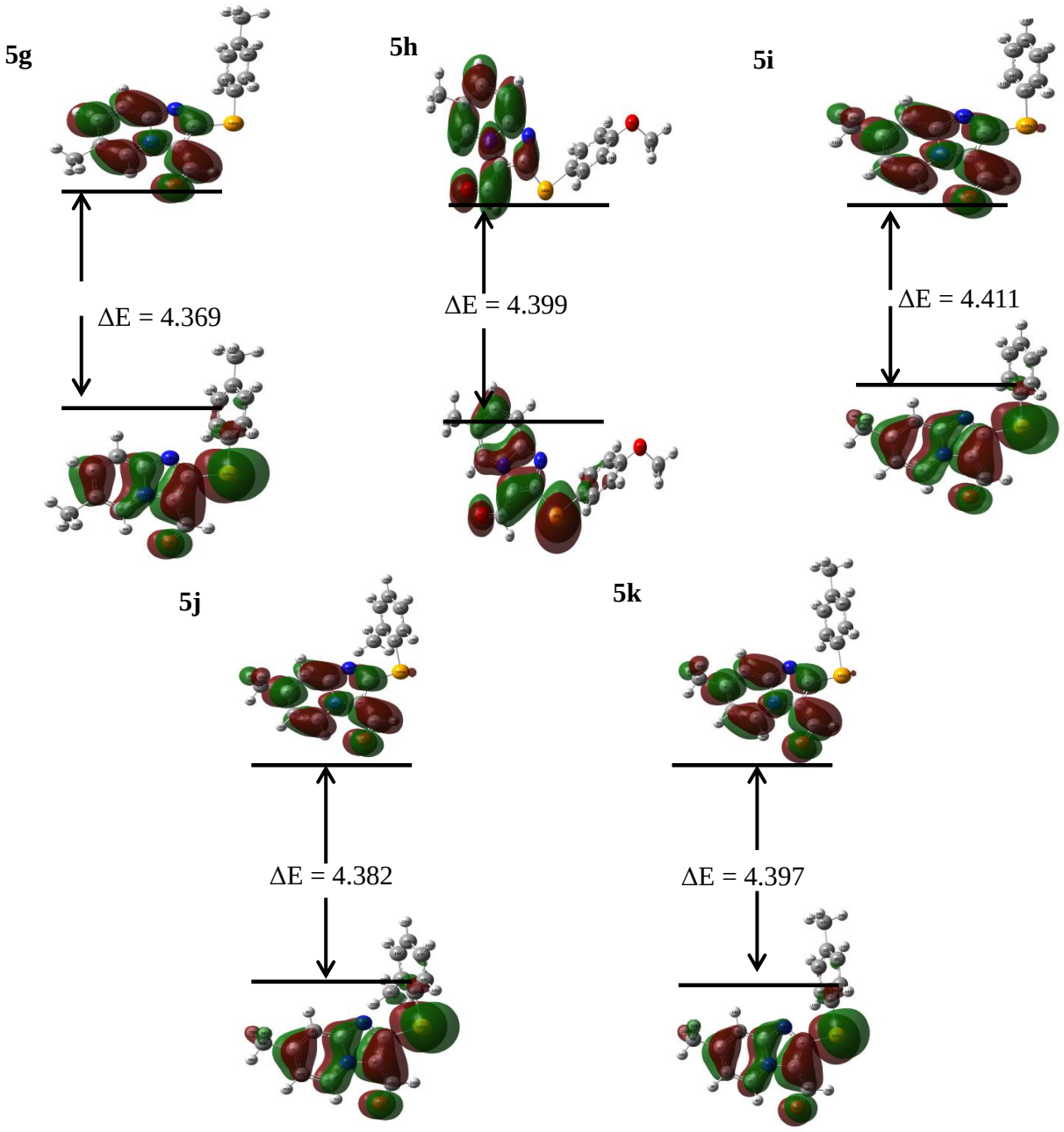


Figure 2. HOMO-LUMO diagram of compounds **5a-f**

Table S3. Antifungal activity of synthesized compounds expressed in MIC (in µg/ml)

Compounds	*C. albicans*	*C. glabrata*	*C. tropicalis*	*C. krusei*	*C. paraposlsis*	*C. Keyfer*	*C. neoformans*	*A. Niger*
5a	>75.25	>75.25	>75.25	>75.25	>75.25	>75.25	>75.25	>75.25
5b	**19.68**	>78.75	**39.37**	>78.75	**39.37**	**39.37**	>78.75	>78.75
5d	**21.43**	**10.71**	>85.75	>85.75	**21.43**	>85.75	>85.75	>85.75
5e	**19.68**	**19.68**	**19.68**	**9.84**	>78.75	39.37	**39.37**	>78.75
5g	>82.25	>82.25	**41.12**	>82.25	>82.25	**41.12**	>82.25	>82.25
5h	>86.25	>86.25	>86.25	>86.25	>86.25	>86.25	>86.25	**43.12**
5i	**19.68**	>78.75	>78.75	**19.68**	>78.75	**19.68**	>78.75	>78.75
5j	>82.25	**20.56**	>82.25	>82.25	**20.56**	>82.25	>82.25	>82.25
5k	>82.25	**20.56**	>82.25	**20.56**	>82.25	**20.56**	>82.25	>82.25
Amphotericin B	0.36	0.18	0.36	0.36	0.36	0.18	0.09	0.18

Table S4. Antibacterial activity of synthesized compounds in MIC (in µg/ml)

Compounds	*E. coli*	*S. aureus*	*E. faecalis*	*L. mono cytogens*	*S. pyogens*	*V. Cholera*
5a	>75.25	>75.25	>75.25	**18.81**	>75.25	>75.25
5b	**39.37**	>78.75	>78.75	**19.68**	>78.75	>78.75
5d	**21.43**	**21.43**	>85.75	>85.75	**42.875**	>85.75
5e	**9.84**	**39.37**	**9.84**	>78.75	**19.68**	**39.37**
5g	>82.25	**41.125**	>82.25	**20.56**	**10.28**	>82.25
5h	**21.56**	>86.25	>86.25	>86.25	>86.25	>86.25
5i	**19.68**	**19.68**	>78.75	>78.75	>78.75	>78.75
5j	**20.56**	**41.125**	>82.25	>82.25	>82.25	>82.25
5k	**20.56**	>82.25	>82.25	**10.28**	>82.25	>82.25
Kanamycin	0.96	7.57	15.14	1.89	15.14	15.14

References:

1. S. Kumar, N. Sharma, I. K. Maurya, A. K. K. Bhasin, N. Wangoo, P. Branda, V. Felix, K. K. Bhasin, R. K. Sharma, *European Journal of Medicinal Chemistry*, 2016, 123, 916-924.